Manual of
Equine
Anesthesia
& Analgesia

Tom Doherty
& Alex Valverde

Manual of Equine Anesthesia and Analgesia

Tom Doherty

College of Veterinary Medicine, University of Tennessee

and

Alex Valverde

Department of Clinical Studies, The University of Guelph

Manual of Equine Anesthesia and Analgesia

Tom Doherty

College of Veterinary Medicine, University of Tennessee

and

Alex Valverde

Department of Clinical Studies, The University of Guelph

Contents

Preface

As in all areas of veterinary practice, equine anesthesia and analgesia have progressed rapidly over the last two decades with the introduction of new drugs, user-friendly monitoring devices and new methods of using drugs. Important knowledge has also been gained in identifying the risk factors for equine anesthesia. There is a growing awareness of the impact of anesthesia and analgesia on the surgical outcome, and a realization that equine anesthesia is not just a technical procedure aimed at producing immobilization for the sake of operator comfort.

This handbook is intended to be a useful clinical guide. The layout has been planned so that the information will be easily accessible, and an attempt has been made to impose some order on the confusion of facts which confront students and clinicians. We hope that we have achieved that goal. Drugs such as chloroform and chloral hydrate, which are rarely used nowadays, have been omitted.

Undoubtedly, not everyone will agree with all the descriptions of how to perform clinical anesthesia as we each have our own preferences. For instance, some readers will not feel comfortable with the multimodal drug approach to general anesthesia. We have emphasized techniques which have, over the years, been found to be effective for the authors. However, we realize that there are other acceptable methods.

It is our sincere hope that this handbook will be a valuable source of information for all involved in equine anesthesia.

Tom Doherty
Alex Valverde

Acknowledgments

Contributors

Dr Benjamin Buchanan DVM, Dip ACVIM
Senior Resident Large Animal Medicine
Department of Large Animal Clinical Sciences,
The University of Tennessee,
College of Veterinary Medicine,
Knoxville,
TN 37996-4545, USA

Dr Rachael E. Carpenter DVM
University of Illinois,
Department of Veterinary Clinical Medicine,
Veterinary Teaching Hospital,
1008 West Hazlewood Drive,
Urbana,
IL 61802, USA

Dr Fernando A. Castro DVM, Dip ACVS
Senior Resident,
Large Animal Surgery,
Department of Large Animal Clinical Sciences,
The University of Tennessee,
College of Veterinary Medicine,
Knoxville,
TN 37996-4545, USA

Dr Nigel Caulkett DVM, MS, Dip ACVA
Professor
Department of Veterinary Anesthesia, Radiology
    and Surgery,
Western College of Veterinary Medicine,
52 Campus Drive,
University of Saskatchewan,
Saskatoon,
Saskatchewan,
S7N 5B4, Canada

Tom Doherty MVB, MSc, Dip ACVA
Department of Large Animal Clinical Sciences,
The University of Tennessee,

College of Veterinary Medicine,
Knoxville,
TN 37996-4545, USA

Dr Lydia Donaldson DVM, PhD, Dip ACVA
P.O. Box 1100,
Middleburg,
VA 20118, USA

Dr Bernd Driessen DVM, DrMedVet.,
Dip ACVA, Dip ECVPT
University of Pennsylvania,
New Bolton Center,
382 W. Street Road,
Kennett Square,
PA 19348, USA

Dr Tanya Duke BVetMed, Dip ACVA
Professor
Department of Veterinary Anesthesia, Radiology
    and Surgery,
Western College of Veterinary Medicine,
52 Campus Drive,
University of Saskatchewan,
Saskatoon,
Saskatchewan,
S7N 5B4, Canada

Dr Christine Egger DVM, MS, Dip ACVA
Associate Professor
Department of Small Animal Clinical Sciences,
The University of Tennessee,
College of Veterinary Medicine,
Knoxville,
TN 37996-4545, USA

Dr Nicholas Frank DVM, PhD, Dip ACVIM
Associate Professor
Department of Large Animal Clinical Sciences,

The University of Tennessee,
College of Veterinary Medicine,
Knoxville,
TN 37996-4545, USA

Dr Deborah Gaon DVM MSc
515-111 Wurtemburg St,
Ottawa,
Ontario
K1N 8M1, Canada

Dr Rebecca Gompf DVM, MS, Dip ACVIM
    (Cardiology)
Associate Professor
Department of Small Animal Clinical
    Sciences,
The University of Tennessee,
College of Veterinary Medicine,
Knoxville,
TN 37996-4545, USA

Dr Tamara Grubb DVM, MS, Dip ACVA
2002 L Schultheis Rd,
Uniontown,
WA 99179, USA

Dr Ralph C. Harvey DVM, MS, Dip ACVA
Associate Professor
Department of Small Animal Clinical Sciences,
The University of Tennessee,
College of Veterinary Medicine,
Knoxville,
TN 37996-4545, USA

Dr Ron Jones MVSc, FRCVS, DVA,
    DrMedVetDip ECVA, Dip ACVA (Hon)
7 Birch Road,
Oxton, Prenton,
Merseyside CH43 5UF,
England

Dr Carolyn Kerr DVM, DVSc, PhD
Department of Clinical Studies,
Ontario Veterinary College,
The University of Guelph,
Guelph,
Ontario,
NIG 2W1, Canada

Dr Leigh Lamont DVM, MS, Dip ACVA
Assistant Professor
Department of Companion Animals,
University of Prince Edward Island,
550 University Avenue,
Charlottetown,
Prince Edward Island,
C1A 4P3, Canada

Dr Casey J. LeBlanc DVM, PhD, Dip ACVCP
Assistant Professor
Department of Pathobiology,
The University of Tennessee,
College of Veterinary Medicine,
Knoxville,
TN 37996-4545, USA

Dr Hui Chu Lin DVM, MS, DACVA
Professor, Anesthesia
Department of Clinical Sciences,
College of Veterinary Medicine,
Auburn University, AL 36849, USA

Dr Alex Livingston B.Vet. Med, PhD, FRCVS
Western College of Veterinary Medicine,
University of Saskatchewan,
52 Campus Drive,
Saskatoon, Saskatchewan,
S7N 5B4, Canada

Dr Elizabeth A. Martinez DVM, MS, Dip
    ACVA
Associate Professor
Department of Small Animal Medicine and
    Surgery,
College of Veterinary Medicine,
Texas A & M University,
College Station,
TX 77843-4474, USA

Dr Craig Mosley DVM, MSc, Dip ACVA
Oregon State University,
Corvallis,
OR 97331-4501, USA

Dr Joanna C. Murrell BVSc, PhD, Dip ECVA
Department of Clinical Sciences of
    Companion Animals,

University of Utrecht, Faculty of Veterinary
  Medicine,
PO Box 80154,
NL-3508 TD Utrecht,
Institute of Veterinary, Animal and Biomedical
  Sciences,
The Netherlands

Dr Hanna-Maaria Palos DVM
Assistant Professor
Department of Large Animal Clinical Sciences,
The University of Tennessee,
College of Veterinary Medicine,
Knoxville,
TN 37996-4545, USA

Dr Frederik Pauwels DVM, MS, Dip ACVS
College of Sciences,
Massey University,
Private Bag 11 222,
Palmerston North,
New Zealand

Dr Robert Reed DVM, PhD
Associate Professor
Department of Comparative Medicine,
The University of Tennessee,
College of Veterinary Medicine,
Knoxville,
TN 37996-4545, USA

Dr Jim Schumacher DVM, MS, Dip ACVS
Professor
Department of Large Animal Clinical Sciences,
The University of Tennessee,
College of Veterinary Medicine,
Knoxville,
TN 37996-4545, USA

Dr Henry Stämpfli DVM, Dip ACVIM
Department of Clinical Studies,
Ontario Veterinary College,
The University of Guelph,
Guelph,
Ontario,
NIG 2W1, Canada

Dr Alex Valverde DVM, DVSc, Dip ACVA
Department of Clinical Studies,
Ontario Veterinary College,
The University of Guelph,
Guelph,
Ontario,
NIG 2W1, Canada

Dr Daniel S. Ward DVM, PhD, Dip ACVO
Professor,
Department of Small Animal Clinical Sciences,
The University of Tennessee,
College of Veterinary Medicine,
Knoxville,
TN 37996-4545, USA

Dr Deborah V. Wilson BVSc, MS, Dip ACVA
Department of Large Animal Clinical Sciences,
Michigan State University,
East Lansing,
MI 48864, USA

List of abbreviations

ACh   acetylcholine
ACT   activated clotting time
AEP   auditory evoked potential
AF   atrial fibrillation
ANS   autonomic nervous system
AP   action potential
aPTT   activated partial thromboplastin time
AST   aspartate aminotransferase
ATIII   antithrombin III
AV   arteriovenous
AVP   arginine vasopressin

BIS   bispectral index
BUN   blood urea nitrogen

CBIL   conjugated (direct) bilirubin
CHF   congestive heart failure
CK   creatine kinase
COX   cyclooxygenase
CPD   citrate-phosphate-dextrose
CPDA-1   citrate-phosphate-dextrose-adenine
CPK   creatinine phosphokinase
CRH   corticotropin releasing hormone
CRI   constant rate infusion
CSF   cerebrospinal fluid
CSHL   context-sensitive half-life
CVP   central venous blood pressure
CVS   cardiovascular system

DA   dopaminergic
DIC   disseminated intravascular coagulation
DMSO   dimethylsulphoxide

ECFV   extracellular fluid volume
ECG   electrocardiogram
ER   exertional rhabdomyolysis
$ETCO_2$ end-tidal carbon dioxide

FDP   fibrin/fibrinogen degradation product

FFT	Fast Fourier transformation
FIO_2	inspired oxygen fraction
FRC	functional residual capacity
FSP	fibrin split product
GABA	gamma amino butyric acid
GFR	glomerular filtration (*or* flow) rate
GGT	gamma glutamyl transferase
GnRH	gonadotropin releasing hormone
GX	glycinexylidine
HR	heart rate
HYPP	hyperkalemic periodic paralysis
ICFV	intracellular fluid volume
ICP	intracranial pressure
IDH	iditol dehydrogenase
IFV	interstitial fluid volume
IPPV	intermittent positive pressure ventilation
IVCT	in vitro contracture testing
LAL	large-animal vertical lift
LP	lipopolysaccharide
MAC	minimum alveolar concentration
MEGX	monoethylglycinexylidine
MH	malignant hyperthermia
MLAEP	middle latency auditory evoked potential
NE	norepinephrine
NMDA	N-methyl-D-aspartate
NSAID	nonsteroidal anti-inflammatory drug
PAB	premature atrial beats
PCV	packed cell volume
PDA	patent ductus arteriosus
PDN	palmar digital nerve
PEEP	positive end-expiratory pressure
PIVA	partial intravenous anesthesia
PLA_2	phospholipase A_2
PNS	peripheral nervous system
PP	perfusion pressure
PPV	positive pressure ventilation
PSSM	polysaccharide storage myopathy
PT	prothrombin time
PV	plasma volume
PVC	premature ventricular contraction
PVR	peripheral vascular resistance

RAO	recurrent airway obstruction
RR	respiratory rate
SA	sinoatrial
SBA	serum bile acids
SCh	succinylcholine
SDH	sorbitol dehydrogenase
SGOT	serum glutamic oxaloacetic transaminase
SID	strong ion difference
SNS	sympathetic nervous system
SV	stroke volume
TBIL	total bilirubin
TBW	total body water
TFPI	tissue factor pathway inhibitor
TIVA	total intravenous anesthesia
TNF_α	tumor necrosis factor-alpha
TOF	train-of-four
TP	total protein
tPA	tissue plasminogen activator
TRH	thyrotropin releasing hormone
TSH	thyroid stimulating hormone
UBIL	unconjugated (indirect) bilirubin
uPA	urokinase plasminogen activator
USG	urine specific gravity
vWD	von Willebrand's disease

1   Preoperative evaluation

The risk of equine anesthesia

Tanya Duke

Most of what is known about the risk of equine anesthesia comes from information gathered in a worldwide, multicenter study, and the following information is based, in large part, on these findings.

I. Risk of equine anesthesia

- Data from *single* clinics have cited the mortality rate in healthy horses to be between 0.63% and 1.8%.
- Data from *multicenter* studies cite the death rate for healthy horses undergoing anesthesia at around 0.9% (approximately 1:100).
- The overall death rate, when sick horses undergoing emergency 'colic' surgery are included, is around 1.9%.
- Surveys of feline and canine anesthesia have documented risk of mortality in healthy patients to be 1:2065 and 1:1483, respectively.
- Clearly, the risk of fatality during anesthesia of healthy horses is greater than for small animals.

II. Risk factors

A. Age
- The risk increases with age, and horses aged 14 years or older are at an increased risk of mortality.
- Older horses may be more prone to fracture of a long bone in the recovery period, resulting in euthanasia.
- Foals have an increased risk of dying and this is speculated to be associated with unfamiliarity with neonatal anesthesia, and presence of systemic illness.

B. Type of surgery
- In otherwise healthy horses, the risk following *fracture* repair is highest.
- This increased risk probably arises from re-fracture and other problems during the recovery period resulting in euthanasia.

- o However, long periods of anesthesia typical of fracture surgery repair have also been associated with increased mortality, and horses presented for fracture repair may be dehydrated and stressed.
- o Emergency surgery (non-colic) carries a 4.25 times higher risk of mortality compared with elective surgery, and for colics the risk of fatality is 19.5%.

C. Time of day

- o Performing anesthesia outside of normal working hours carries an increased risk for horses. This increase in risk is separate from the fact that most of these cases are emergency in nature.
- o Surgeries performed between midnight and 6 a.m. carry the highest risk of mortality. This may be due to the nature of the emergency, as well as to staff shortages and tiredness.

D. Body position

- o This has not been found to increase risk after including operation type in the analysis, since most 'colic' surgeries are performed with the horse in dorsal.

E. Drug choice

- o Using total inhalational anesthesia regime in foals (<12 months of age) *without premedication* carries the highest risk.
- o *Halothane*, which sensitizes the myocardium to circulating catecholamines, may have a higher risk than newer volatile anesthetics.
- o Not using any premedication is associated with the highest risk, probably owing to increased circulating catecholamines from stress.
    - – It may be prudent to premedicate foals before induction of anesthesia.
- o *Acepromazine* lowers the risk of mortality, when it is used on its own as a premedicant. This may be due to *acepromazine*'s stabilizing effect on the heart, making it less susceptible to ventricular arrhythmias.
- o No particular injectable induction regime is associated with greater risk when used with inhalational anesthesia.
- o Total intravenous anesthesia (TIVA) is associated with the lowest risk of all, but this may be due to the fact that TIVA is used for shorter procedures.

F. Duration of anesthesia

- o Long periods of anesthesia with volatile anesthetics are often associated with cardiovascular depression and poor tissue perfusion leading to problems such as cardiac arrest or post-anesthetic *myopathy*.

Preoperative evaluation and patient preparation

I. Risk management

- Those of us involved in equine anesthesia are in the risk management business.
- Anesthesia of the horse is never without risk.
- The risks range from the less serious (e.g. skin wounds) to the more serious (e.g. myopathies and peripheral neuropathies) and to death in some cases.
- There is also a risk to personnel and this should never be taken lightly.
- The *goal of the anesthesiologist* is to minimize the adverse effects of these risks (ideally at minimum cost) by:
  ○ Identifying and defining the risk(s).
  ○ Selecting the best strategy for controlling or minimizing the risk(s).

II. Classification of physical status

- Classification of health status is generally based on the American Society of Anesthesiologists (ASA) system.
- This system uses information from the history, physical examination and laboratory findings to place patients into one of five categories.
- The classification allows for standardization of physical status only.
- The ASA system does *not* classify risk.
- These classifications are not as useful for equine patients; nevertheless, the system serves as a guide.

ASA 1   A healthy horse.
ASA 2   Horse with mild systemic disease (e.g. mild anemia, mild recurrent airway obstruction).
ASA 3   Horse with severe systemic disease (e.g. severe recurrent airway obstruction).
ASA 4   A horse with severe systemic disease that is a constant threat to life (e.g. ruptured urinary bladder, intestinal accident).
ASA 5   A moribund horse not expected to survive longer than 24 hours (e.g. foal with a uroperitoneum with severe metabolic derangements).
E   The letter E is added to each classification for emergency procedures.

III. Patient preparation

A. Evaluation

  ○ The horse should be evaluated in light of its *history* and *physical findings*.
  ○ Many emergency cases, especially intestinal emergencies, are in cardiovascular shock and must be resuscitated prior to induction of anesthesia.
  ○ If deemed necessary, *laboratory data* are important in order to determine suitability for anesthesia and to determine the risk.

B. Laboratory tests

○ In normal horses undergoing elective surgery, there is generally no value in performing laboratory tests.
○ In emergency cases, performing laboratory tests may be vital to the management of the case (e.g. a foal with urinary bladder rupture).

C. Physical examination

○ During the examination, particular attention should be directed to the cardiovascular and respiratory systems.
○ Musculoskeletal problems, which may affect recovery, should be considered, and a plan should be made to assist recovery if deemed necessary.

D. History

○ May reveal information that affects case management.
○ A recent history of coughing may indicate a viral infection of the airway, in which case elective surgeries should be postponed until one month following resolution of clinical signs.
○ Owners often report that the horse has previously had a 'bad' or 'over' reaction to some anesthetic drug. In most cases these are misunderstandings on the part of the owner, but they should nevertheless be noted.

E. Fasting

○ Fasting (~ 12 h) was previously advised because of the potential benefits for lung function and the reduced risk of stomach rupture from trauma at induction or recovery.
○ Some clinicians question this reasoning and many equine hospitals *do not fast* horses prior to elective surgery.
  – There is also a concern that fasting may increase the risk of postoperative ileus, although there is no evidence to support this.

F. Medications

○ It is best to administer all ancillary drugs (e.g. antimicrobials, anti-inflammatories) prior to sedation.

G. Jugular catheter

○ An intravenous catheter should *always* be placed prior to anesthesia.
○ This reduces the likelihood of perivascular injection and provides ready access to the vein, for medication administration, in emergency situations.

H. Flushing the oral cavity

○ It is important to flush food debris from the oral cavity, especially if the airway is going to be intubated.

I. Removal of shoes

- o Removal of shoes is sometimes practiced to prevent damage to the horse and hospital flooring.
  - – However, removal of shoes is not popular with owners. An alternative is to apply bandage material or tape to improve grip and cover metal points.
- o Certainly, loose shoes and nails should be removed.

Serum chemistry testing prior to anesthesia

Nicholas Frank

- Ideally, routine serum chemistry results should be examined before general anesthesia is induced.
  - o These values are particularly useful for assessing problems that cannot be recognized by physical examination.
  - o For instance, a horse suffering from acute renal failure may appear healthy upon physical examination, but disease is revealed when serum blood urea nitrogen and creatinine concentrations are examined.
- This discussion focuses upon four body systems (muscle, liver, kidneys and plasma proteins) that should be assessed prior to anesthesia by examining serum chemistry values.
- Reference ranges are provided for each of the variables discussed, but clinicians are advised to use reference ranges provided by their laboratory.

I. Muscle

A. Creatine kinase (CK)

- o Also called creatinine phosphokinase (CPK).
- o Specific indicator of muscle damage.
  - – *Leakage* enzyme released when myocytes rupture.
  - – CK has a short half-life (hours), so serum concentrations fall quickly after an episode (indicates *acute*, *ongoing* muscle damage).
- o This enzyme catalyzes the transfer of high-energy phosphate groups from ATP to creatine during exercise, and then the reverse reaction occurs during rest.
- o Reference range: 60–330 U/liter.
- o *Mildly increased* (< 1000 U/liter):
  - – If the horse is recumbent or rolling.
  - – Can also be detected after recent exercise or if the horse has just arrived by trailer.
  - – If the previous conditions do not apply, then mild exertional rhabdomyolysis (ER) and/or polysaccharide storage myopathy (PSSM) should be suspected.
- o *Moderately* (> 1000 U/liter) to *severely increased* (> 10 000 U/liter):
  - – If the horse is currently suffering from ER:
    - ■ Urine should be checked for myoglobin.
    - ■ Intravenous fluids should be administered to promote diuresis.

B. Aspartate aminotransferase (AST)

- o Previously called serum glutamic oxaloacetic transaminase (SGOT).
- o Indicator of *muscle damage* or *liver damage*.
  - – *Leakage* enzyme released when *myocytes* or *hepatocytes* rupture.
  - – Long half-life (days), so serum concentrations fall slowly after an episode.
- o This enzyme is involved in amino acid degradation.
- o Reference range: 160–412 U/liter.
- o Muscle damage affects AST and CK if the disease process is ongoing.
  - – However, serum AST activity will remain increased after CK activity has returned to normal.
- o *Increased AST activity* indicates a previous ER episode or suggests the presence of PSSM.

II. Liver

- • Chronic liver diseases such as *pyrolizidine alkaloid toxicosis* or *cholelithiasis* can go undetected unless serum chemistry values are examined.
  - o This is particularly true in horses because the finding of icterus is often discounted as a consequence of reduced food intake.
- • Presence of one of these diseases may significantly alter the overall prognosis for the patient and should be discussed with the client prior to anesthesia.
- • Hepatic dysfunction must be recognized prior to anesthesia because this condition may alter the metabolism of certain anesthetic agents.

A. Gamma glutamyl transferase (GGT)

- o Specific indicator of liver damage.
  - – *Inducible* enzyme released when cells become stressed.
  - – Bile accumulation (cholestasis) and certain drugs (e.g. phenobarbital) increase serum GGT activity.
  - – GGT has a long half-life (days), so serum concentrations fall slowly after an episode.
- o This enzyme is found within the membranes of hepatocytes and is most abundant within the biliary epithelial cells.
- o It is involved in glutathione metabolism.
- o Reference range: 6–32 U/liter.
  - – The normal range for *burros*, *donkeys* and *asses* may be 2–3 times higher.
- o Cholestasis can result from intra- and extrahepatic causes.
  - – *Intrahepatic cholestasis* accompanies chronic liver diseases such as pyrolizidine alkaloid toxicosis and cholelithiasis. Acute and subacute liver diseases also cause intrahepatic cholestasis when hepatocytes swell and compress bile ductules.
  - – *Extrahepatic cholestasis* occurs when the common bile duct is occluded by choleliths, or when bile flow is impaired by inflammation of the bile duct papilla within the duodenum.
    - ■ Horses that are accumulating gastric reflux as a result of enteritis may also have increased GGT activities and hyperbilirubinemia because bile is not being transported away by the ingesta.

■ Cholestasis sometimes accompanies displacement of the large colon because the common bile duct courses through the duodenocolic ligament, which becomes stretched.

B. Sorbitol dehydrogenase (SDH)

○ Also called iditol dehydrogenase (IDH).
○ Requires special handling.
  – SDH is not offered on most routine serum chemistry panels, but can be easily requested.
○ Specific indicator of *liver damage*.
  – *Leakage* enzyme released when hepatocytes rupture.
  – SDH has a short half-life (hours), so serum concentrations fall quickly.
○ This enzyme is found within the cytosol of hepatocytes and plays a role in a glucose metabolism pathway that bypasses glycolysis.
○ Reference range: 1–8 U/liter.
○ *Increased activity* indicates ongoing hepatocellular injury because SDH concentrations fall quickly as the disease resolves.

C. Aspartate aminotransferase (AST)

○ Found on most serum chemistry panels, so can be evaluated if SDH is not available.
○ Indicator of *muscle damage* or *liver* damage.
  – Leakage enzyme released when myocytes or hepatocytes rupture.
○ Reference range: 160–412 U/liter.

D. Total bilirubin (TBIL)

○ Indicator of *hepatic dysfunction*, *hemolysis*, or *reduced feed intake*.
○ Waste product of heme. Aged or defective erythrocytes are removed from circulation by the spleen and heme is catabolized to bilirubin within macrophages.
  – Unconjugated (indirect) bilirubin (UBIL) is released, which circulates in the blood bound to albumin.
  – Circulating UBIL is removed from the blood by the liver and conjugated with glucuronic acid to improve water solubility.
  – Conjugated (direct) bilirubin (CBIL) is excreted in the bile.
○ TBIL concentration is commonly reported, but this value may be subdivided into UBIL and CBIL fractions.
○ Reference range (TBIL): 0–3.2 mg/dl (0–54.7 µmol/liter).
○ *Hepatic dysfunction* causes UBIL and CBIL concentrations to rise.
○ *Biliary obstruction* (e.g. cholelithiasis) raises the CBIL to UBIL ratio.
○ *Hemolysis* raises the serum UBIL concentration because erythrocytes are either lysed in circulation (intravascular hemolysis), or cleared more rapidly from the blood (extravascular hemolysis). Free hemoglobin is metabolized by hepatocytes.
○ *Reduced food intake* also raises the serum UBIL concentration, but this time as a result of slowed clearance of bilirubin from the blood instead of overproduction. Free fatty acids, released in greater quantities in response to negative energy balance, are thought to compete with UBIL for carrier proteins that facilitate entry into hepatocytes.

E. Serum bile acids (SBA)

○ Requires special handling.
○ Indicator of hepatic dysfunction.
○ Reference range: 0–20 μmol/liter.
○ Bile acids are synthesized and secreted by the liver, so it at first seems logical to assume that SBA concentrations decrease as hepatic function declines. However, this is *not the case* because greater than 90% of bile acids excreted via the bile into the duodenum are subsequently reabsorbed by the intestine and used again by the liver (enterohepatic circulation). Bile acids are removed from the portal blood by hepatocytes, so *SBA concentrations increase as hepatic function decreases*.
○ Only a single blood sample is required instead of pre- and post-feeding samples because the horse does not have a gallbladder and releases bile continuously.

III. Kidneys

● Detection of pre-renal azotemia or renal failure prior to anesthesia alerts the clinician to the need for intravenous fluids and blood pressure support during the procedure.
  ○ Renal failure affects the prognosis for the patient and should therefore be discussed with the client.

A. Blood urea nitrogen (BUN)

○ Indicates that the horse suffers from pre-renal, renal, or post-renal azotemia (this term is also commonly used when serum creatinine concentrations are increased).
○ Reference range: 10–25 mg/dl (3.6–8.9 mmol/l).
○ BUN is synthesized by the liver and excreted via the kidneys.
○ It is a waste product of amino acid catabolism.

Pre-renal azotemia
○ Occurs when the glomerular filtration rate (GFR) has been decreased by a reduction in renal perfusion.
○ Dehydration and circulatory shock are the most common causes of pre-renal azotemia.
○ Prolonged renal hypoperfusion can lead to renal failure, so this problem should be addressed expeditiously.
○ When renal function is adequate (pre-renal), azotemia is accompanied by a urine specific gravity (USG) > 1.025 g/ml (i.e. the urine is concentrated).
○ Uroperitoneum secondary to *bladder rupture in foals* also causes pre-renal azotemia.

Renal azotemia
○ Occurs when the GFR is low as a result of acute or chronic renal failure.
○ Renal azotemia is diagnosed by concurrently measuring the urine specific gravity.
○ Renal failure is defined by the presence of azotemia in a patient that cannot concentrate its urine (USG < 1.025 g/ml).

Post-renal azotemia
- o Is associated with mechanical (e.g. uroliths) or functional (e.g. neurogenic bladder dysfunction) obstruction of the urinary tract.

B. Creatinine

- o Usually examined with BUN (pre-renal, renal, or post-renal azotemia).
- o Reference range: 0.4–2.2 mg/dl (35.4–194.5 µmol/liter).
- o Creatinine is synthesized from creatine (found in muscle) by a nonenzymatic irreversible reaction at a constant rate and then excreted via the kidneys.
- o Is freely filtered by the glomerulus.
  - – In contrast with urea nitrogen, creatinine is *not reabsorbed* within the tubules, so serum creatinine concentrations provide a more accurate measurement of GFR.

IV. Plasma proteins

- Hypoproteinemia cannot be detected upon physical examination of the horse unless subcutaneous edema is observed, or wheezes consistent with pulmonary edema are auscultated.
  - o These abnormalities are unlikely to be present when hypoproteinemia is first developing and may only become apparent when intravenous fluids are administered to correct dehydration.
- It is therefore imperative that, at least, the patient's plasma total protein concentration be examined.
- A *refractometer* can be used to measure total solids, but it is preferable to examine serum total protein (TP), albumin, and globulin concentrations provided on a *serum chemistry panel*.
- Albumin and globulin concentrations should be examined individually because hyperglobulinemia can accompany chronic disease in horses and prevent hypoalbuminemia from being detected when only a serum total protein concentration is examined.

A. Total protein

- o Reference range (serum): 5.6–7.6 g/dl (56–76 g/l).
- o Reference range (plasma): 6.0–8.5 g/dl (60–85 g/l).
- o In the author's experience, most horses fall within a range of 6.0–7.0 g/dl.

B. Albumin

- o This protein is synthesized by the liver and has a plasma half-life of 19 days.
- o Reference range: 2.6–4.1 g/dl (26–41 g/liter).
- o Albumin accounts for 75% of *oncotic* activity within the plasma.
- o *Edema* develops as consequence of *hypoalbuminemia*, and the rate of progression depends upon the degree of hypoalbuminemia and how quickly it developed.
  - – Generally, plasma or whole blood transfusion is considered when serum or plasma albumin concentrations approach 1.5 g/dl.

Four general causes of hypoalbuminemia
- o Low dietary protein intake.
- o Reduced synthesis by the liver.
- o Excessive catabolism (as occurs with starvation).
- o Increased loss from the blood.
  - – The most common cause.
  - – Examples include:
    - ■ Loss into the lumen of the gastrointestinal tract with bacterial colitis or strangulation of the bowel.
    - ■ Loss into the abdomen with peritonitis.
    - ■ Loss into the thoracic cavity with pleuropneumonia.
    - ■ Loss into subcutaneous tissues as a result of vasculitis.
    - ■ Loss through the glomerulus when damage occurs at this site.

C. Globulins

- o Include α, β, and γ globulins.
- o These proteins are larger in size than albumin and are synthesized by various cells including hepatocytes (haptoglobin) and plasma cells (IgG).
- o Reference range: 2.6–4.0 g/dl (26–40 g/liter).
- o *Hyperglobulinemia* is associated with chronic disease, and should alert the clinician to the presence of a nidus of inflammation such as a tumor or abscess. This finding is unlikely to impact anesthesia, but may affect the overall outcome of the case.

2   The cardiovascular system

Physiology of the cardiovascular system

Tamara Grubb

- The cardiovascular system consists of three components (heart, vessels, blood) whose ultimate goal is to deliver oxygen to the working cells.
- Tissue oxygen delivery (DO_2) is determined by the amount of blood pumped to the cells (cardiac output or 'Q') and the oxygen content of the blood (CaO_2).
- Anesthesia can drastically alter cardiovascular function and have a global impact on organ function via decreased DO_2. Thus, a working knowledge of normal cardiovascular function is important.

I. Anatomy

A. Chambers

- The equine heart is a typical mammalian heart with four chambers: two atria and two ventricles.

Atria
- Primary function is to receive and store blood that will empty into the ventricles during early diastole.
- Oxygen-depleted blood from the body is delivered to the right atrium via the cranial and caudal vena cavae and from the myocardium via the coronary sinus and cardiac veins.
- Oxygen-rich blood from the lungs is delivered to the left atrium via pulmonary veins.

Ventricles
- Primary function is to pump blood into the high-pressure systemic (left ventricle) and low-pressure pulmonary (right ventricle) circulations.
- As described by the *Law of LaPlace*, the thick-walled, conical left ventricle is better suited for high-pressure pumping than the thin-walled, flattened, right ventricle.

Atrioventricular valves
- Connect atria and ventricles.
- Tricuspid valve between right atrium and ventricle.
- Mitral valve between left atrium and ventricle.

Semilunar valves
- ○ Connect ventricles to outflow tracts.
- ○ Aortic valve between left ventricle and aorta.
- ○ Pulmonary valve between right ventricle and pulmonary artery.

B. Structural or 'skeletal' components of the heart

- ○ *Myocardium* – muscle layer (striated muscle) of atria and ventricles.
- ○ *Endocardium* – internal lining of the heart chambers, valves and blood vessels.
- ○ *Epicardium* – external lining of the myocardium, continuous with pericardium; secretes pericardial fluid.

C. Neural input to the heart

- ○ Atria are highly innervated by sympathetic and parasympathetic fibers.
  - – Parasympathetic – decrease rate and contractility.
  - – Sympathetic – increase rate and contractility.
- ○ Ventricles are primarily innervated by sympathetic fibers.
  - – Continually discharge to maintain a strength of ventricular contraction 20–25% greater than what would occur with no sympathetic input.

II. Cardiac contractions

A. Initiation

- ○ Unlike most systems in the body, neither the autonomic nor motor neurons are necessary for *initiating* cardiac contractions.
- ○ The heart can continue beating in the absence of outside neural control because the cells of the *specialized electrical conducting system* of the heart are capable of automatic rhythmical depolarization or 'self-excitation'. This is due to:
  - – Cell membranes that are 'leaky' or permeable to sodium.
    - ■ Increased permeability to potassium and calcium ions also plays a role in the spontaneous depolarization of the pacemaker cells.
  - – A *resting* cell membrane potential that is not negative enough to keep sodium channels closed.
    - ■ The resting membrane potential of cardiac conducting cells is −60 to −70 millivolts (mV) and that of the sinoatrial node is −55 to −60 mV (compared with −90 mV for normal muscle cell membranes).

B. Components of the specialized electrical conducting system

- ○ Sinoatrial (SA) node:
  - – Has the fastest rate of spontaneous depolarization and is the *pacemaker*.
  - – Located at the junction of the cranial vena cava and the right auricle.
- ○ Atrioventricular (AV) node:
  - – Slows the rate of impulse transmission as it conducts impulses from the atria to the ventricles.

- o   Internodal pathways:
    - –   Conduct impulses through the atria to the AV node.
- o   Right and left bundle branches and His–Purkinje system.
    - –   Conduct impulses throughout ventricles and ventricular septum.

III. Unique features of the equine heart

- ●   Large SA node.
    - o   A wandering pacemaker is common.
        - –   Seen as *variably shaped P waves* on electrocardiogram (ECG).
- ●   Large atria that may depolarize slightly asynchronously.
    - o   Result in *biphasic P waves* on the ECG.
- ●   Deeply penetrating His–Purkinje system.
    - o   Facilitates movement of electrical impulses throughout the large ventricular muscle. Often called Type II Purkinje system.
- ●   Ossa cordi.
    - o   In all species there is a connective tissue 'skeleton' that separates the atria from the ventricles.
    - o   In cattle and in older horses, these structures may ossify and create two bones, the 'ossa cordi'.

IV. Circulatory systems

- ●   The *systemic* (high pressure) and *pulmonary* (low pressure) circulatory systems are separate but coupled (in series) and interdependent so that dysfunction of one will lead to dysfunction of the other.
- ●   The circulatory systems are not mere conduits; through *dilation* and *constriction*, they control distribution of blood throughout the body and in localized tissue beds.
- ●   The lymphatic system is often included as a component of the circulatory system.

A. Components of the systemic circulation

Aorta → Arteries → Arterioles → Capillaries → Venules → Great veins → Right atrium

- o   The elastic wall of the *aorta* recoils following ventricular contraction, creating a force that maintains blood flow throughout both systole and diastole.
- o   *Arterioles* provide the greatest resistance to circulation and, via dilation or constriction, control blood flow to each tissue capillary bed.
- o   *Capillaries* are the site of exchange of nutrients and waste products.
- o   The majority of the circulating blood volume (approximately 80%) is generally 'stored' in the *venules* and *great veins*.

B. Components of the pulmonary circulation

Pulmonary artery → Arterioles → Capillaries → Pulmonary vein → Left atrium

- ○ The *pulmonary artery* is the only artery in the body that carries deoxygenated blood, and the pulmonary vein is the only vein that carries oxygenated blood.
- ○ Although the pulmonary circulation receives the same cardiac output as the systemic circulation, the pulmonary system remains a low-pressure system due to the:
  - – Tremendous distensibility of the thin-walled vessels.
  - – Large number of vessels that aren't normally perfused but which can be recruited in times of increased output.
- ○ Distribution of pulmonary blood vessels is an important component of ventilation/perfusion (V/Q), distribution and gas exchange.
- ○ Unlike most tissues in the body, pulmonary tissues constrict when hypoxic (*hypoxic pulmonary vasoconstriction*) in an attempt to divert blood away from poorly ventilated alveoli.
  - – This phenomenon can contribute to V/Q mismatch, especially during anesthesia.
- ○ The lung also receives blood flow through the bronchial circulation, a branch of the systemic circulation that perfuses the tissues of the respiratory system.

C. Blood

- ○ Consists of plasma and cellular components.
- ○ Normal equine hematocrit or packed cell volume (PCV) is approximately 35–45% and normal hemoglobin is approximately 15 g/dl.
  - – Most oxygen is transported bound to hemoglobin. (See section on DO_2.)
  - – When saturated, equine hemoglobin binds 1.36–1.39 ml of oxygen per gram of hemoglobin.

V. Cardiovascular physiology

- • The *cardiac cycle* can be described as a period of ventricular contraction (*systole*) followed by ventricular relaxation (*diastole*).
- • The electrical, mechanical and audible events that occur during the cardiac cycle are depicted in the Wiggers diagram (see Fig. 2.1) and described below.

A. Events occurring during late diastole

- ○ The cardiac cycle begins with the spontaneous discharge of the pacemaker, the SA node.
- ○ Discharge is followed quickly by electrical activation of the right atrial muscle and then the left atrial muscle.
  - – This results in the *P wave* on the ECG.
  - – Passive filling of the ventricles occurs during this period.
  - – Because electrical activation always precedes mechanical activity (termed the *electromechanical delay*), the actual atrial contraction occurs shortly after the P wave is generated.
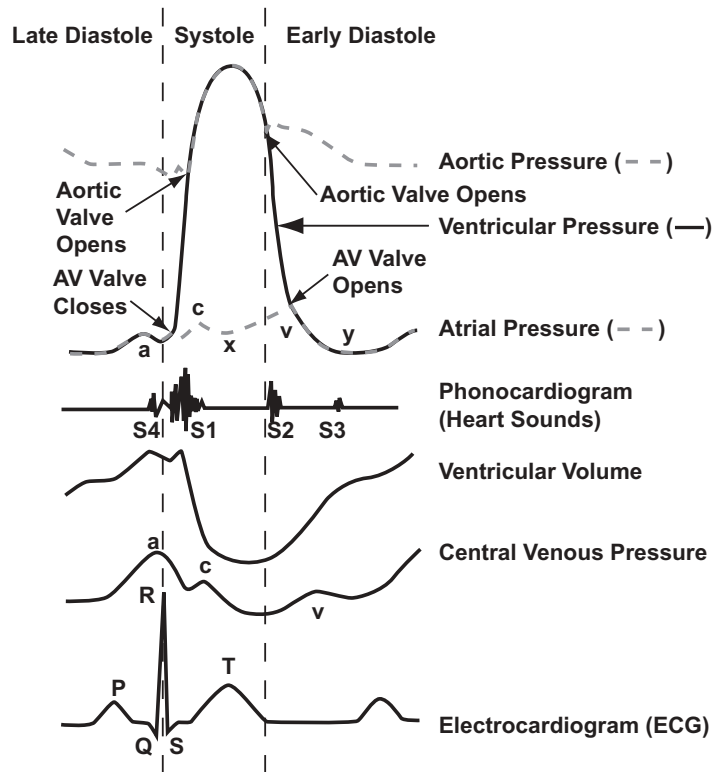
Fig. 2.1 Wiggers diagram demonstrating the events in the cardiac cycle.

- ○ The rapid flow of blood from atrium to ventricle following atrial contraction generates the *atrial* or *fourth heart sound* (S4) and adds blood to the ventricles so that *end-diastolic blood volume* (or *preload*) is reached.
    - – The atrial contribution to the ventricular blood volume is generally minimal and not affected by atrial arrhythmias such as atrial fibrillation.
    - – However, during high heart rates when the diastolic filling time is shortened and in patients with impaired contractility and decreased stroke volume, the atrial contribution becomes a significant percentage of the total ventricular volume and subsequent ejection fraction.
- ○ Atrial contraction causes a rise in atrial pressure (*'a' wave*) which is transmitted up the systemic venous system and often produces a normal *jugular pulse*.
- ○ The atrial excitation wave reaches the medial wall of the right atrium and is conducted slowly through the AV node.
    - – This results in the *PR interval* on the ECG.
    - – *AV block* occurs when the impulse from the atria is not conducted through the AV node to the ventricles.
        - ■ This is reflected on the ECG as a P wave that is not followed by a QRS.
        - ■ In the horse, AV block is generally normal and is due to inherently high *vagal tone*.
        - ■ This is considered benign if the block is abolished by exercise or excitement.

B. Events occurring during systole

- o The impulse exits the AV node and electrical activation of the ventricles occurs.
    - – This results in the *QRS complex* on the ECG.
- o Ventricular contraction begins shortly after electrical activation.
    - – Ventricular pressure quickly exceeds atrial pressure.
- o AV valves are forced closed, producing the high-frequency *first heart sound* (S1).
    - – Following closure of the AV valves and prior to the onset of ventricular ejection, the ventricle contracts on a constant volume of blood (*isovolumetric contraction*).
- o When left ventricular pressure exceeds aortic and pulmonary artery pressure, the *semilunar valves* open and ventricular ejection (the *ejection period*) begins.
    - – The time between the onset of the QRS and the opening of the semilunar valves (the *pre-ejection period*) can be measured by echocardiography and is an index of ventricular myocardial contractility.
    - – Normal functional systolic flow or *ejection murmurs* may occur during the early part of the ejection period.
    - – The *arterial pulse* can be palpated during the ejection period, but the actual timing of the pulse depends on the proximity of the palpation site relative to the heart.
- o The audible *cardiac impulse* or *apex beat* occurs during early systole when the contracting heart twists slightly, causing the left ventricle to strike the chest wall just caudal to the left olecranon.
- o A *'c' wave* will be observed during early systole due to bulging of the tricuspid valve into the right atrium or possibly due to pulsations from the carotid artery.
- o Ventricular contraction causes the atria to collapse towards the ventricles (*ventricular suction*), which causes a brief collapse of the jugular vein and a decrease in atrial pressure (the *'x' descent*).
- o Following this event, atrial filling begins.
    - – This generates the positive *'v' wave*.

C. Events occurring at the end of the ejection period (late systole/early diastole)

- o Ventricular pressure rapidly drops below the pressure in the aorta and pulmonary artery, causing a reversal of the direction of blood flow and closure of the *semilunar valves*.
    - – This produces the high-frequency *second heart sound* (S2).
    - – In horses, the pulmonary valve may close either slightly after or slightly before the aortic valve, resulting in an audible *splitting* of S2. This splitting is normal but can be dramatic in horses with pulmonary disease.
    - – Along with aortic recoil, valve closure produces the *incisura* of the arterial pressure curve.

Comment: The amount of blood ejected during systole is called *stroke volume* and the ratio of the stroke volume to the end-diastolic volume is the *ejection fraction*, which is a commonly used measure of systolic function.

D. Events occurring during early diastole

- o Ventricular pressure continues to fall with no change in ventricular volume (*isovolumetric relaxation*).

o   This proceeds until ventricular pressure drops below atrial pressure, at which time the AV valves open and the phase of *rapid ventricular filling* begins.

–   Ventricular pressure rises slowly, but ventricular volume increases rapidly as blood that accumulated in the atria during ventricular systole flows rapidly into the ventricle.

–   Rapid filling may be associated with a *functional protodiastolic murmur*, and the termination of rapid filling results in the low-frequency *third heart sound* (*S3*).

–   The rapid decline in atrial volume and pressure results in the '*y*' *descent* on the atrial pressure curve and may be visualized as a collapse of the jugular vein.

o   The period of rapid ventricular filling is followed by a period of low velocity filling (*diastasis*) which extends until the next atrial systole.

–   In the resting horse with a normal heart rate, diastasis is the longest period of diastole.

–   During diastasis, jugular vein filling may occur, especially during periods of bradycardia.

o   *SA node firing* followed by *atrial contraction* occur during the last phase of ventricular diastole and start the cardiac cycle again.

VI. Cardiovascular function and clinical applications

●   Clinically, cardiovascular function is determined by measurable components such as heart rate, blood pressure and cardiac output.

●   Anesthetic drugs, surgical positioning, surgical events (e.g. hemorrhage) and pathology prior to surgery (e.g. sepsis) can have a profound effect on cardiovascular function.

A. Cardiac output

$$\text{Cardiac output} = \text{HR} \times \text{SV}$$

o   Defined as the volume of blood ejected by the ventricles per minute (liters/min).

o   Equals the product of heart rate (HR, beats/min) and stroke volume (SV, liters/beat).

o   In a normally functioning heart, cardiac output equals venous return.

o   Cardiac output in the conscious resting horse (400–500 kg) is 32–40 liters/min.

o   To standardize cardiac output among individuals, it is often normalized for body surface area or body weight and reported as *cardiac index*.

–   Cardiac index in the conscious, resting horse is 70–90 ml/kg/min.

Factors affecting cardiac output

o   Heart rate.

o   Preload.

o   Afterload.

o   Contractility.

B. Heart rate

- o   Horses have a wide heart-rate range.
  - –   A resting low rate of 24–40 beats/min to a high of 220–240 beats/min at exercise.
- o   Increased heart rate will generally result in increased cardiac output if stroke volume is constant.
  - –   In horses, the largest changes in cardiac output generally occur due to a change in heart rate (rather than in stroke volume).
  - –   Extreme *tachycardia* may actually decrease cardiac output because diastolic filling time is decreased, resulting in decreased stroke volume.
- o   Extreme tachycardia may cause arrhythmias and worsen cardiac disease since the rapidly beating heart spends less time in diastole, the period of the cardiac cycle in which the myocardium itself is perfused.
- o   During tachycardia, *myocardial oxygen delivery* is decreased at a time when *myocardial oxygen consumption* is increased, resulting in inadequate oxygen delivery to the myocardium (i.e. oxygen debt).

Factors influencing heart rate

- o   Heart rate is primarily regulated by autonomic input.
  - –   Parasympathetic (decreases) and sympathetic (increases).
  - –   Horses have inherently *high vagal tone* which contributes to their slow resting heart rate and normally occurring intermittent second-degree AV block.
- o   Heart rate is also affected by factors such as ambient temperature, body temperature, exercise, pain, fever and anemia, and reflexively controlled by blood pressure through baroreceptor responses.
- o   Various other influences also affect heart rate.
  - –   For instance, the *Bainbridge reflex* is an increase in heart rate secondary to increased right atrial volume and stretching of the SA node.
- o   Anesthetic drugs can affect heart rate directly or indirectly.
  - –   Anticholinergics (e.g. *atropine*) decrease parasympathetic tone and increase heart rate.
  - –   Alpha$_2$ agonists (e.g. *xylazine*) decrease heart rate via direct effects on the SA node and indirect effects via the baroreceptor response.
    - ■   Alpha$_2$ agonists cause vasoconstriction and hypertension.
  - –   *Acepromazine* and inhalational anesthetic agents may cause hypotension, which could, in turn, lead to a baroreceptor-mediated increase in heart rate.

C. Stroke volume (SV)

- o   Defined as the volume of blood ejected by the ventricles per beat.
  - –   SV = (*end-diastolic ventricular volume*) − (*end-systolic ventricular volume*).
- o   SV is a product of *preload*, *afterload* and *contractility* (inotropy).
  - –   These components are interlinked and interdependent.

Preload

- o   Is the force acting to stretch the ventricular fibers at the end of diastole.
- o   May be described as either *end-systolic volume* or *end-systolic pressure*.
- o   The volume or pressure in the *left ventricle* is generally used to determine preload.
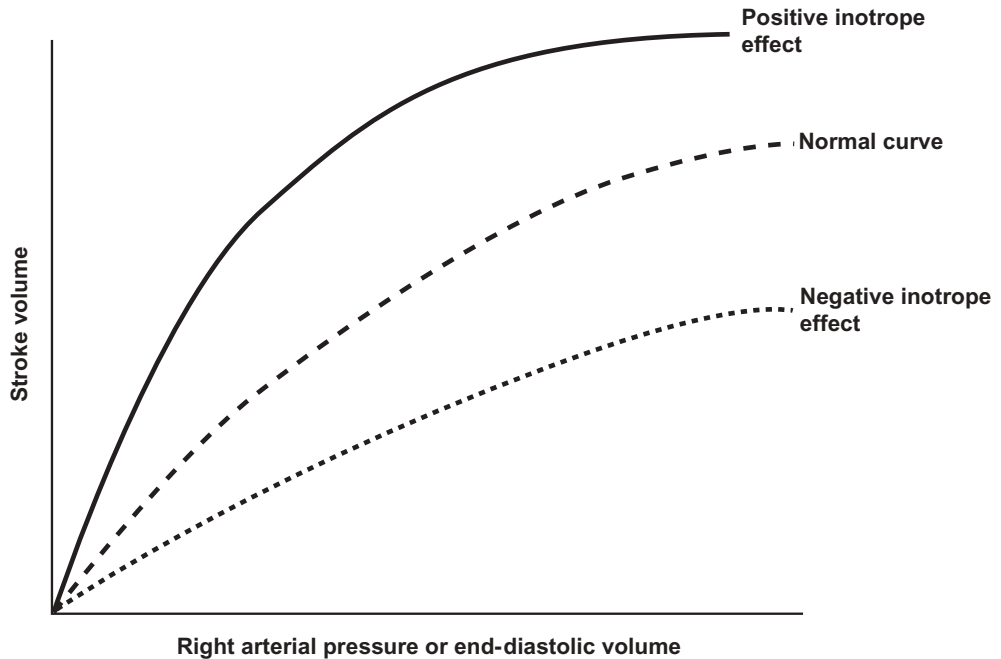
Fig. 2.2   Frank–Starling curve depicting stroke volume as a function of preload. The effects of positive and negative ionotropes on stroke volume are also shown.

- o Dictated in large part by *venous return*.
  - – The venules serve as *capacitance vessels* or reservoirs, storing the majority of the circulating blood volume. They constrict during times of increased demand, thereby increasing venous return and preload. The great veins and the spleen also act as reservoirs for blood.
  - – Anesthetic agents that can change venous return include *acepromazine* (via vasodilation) and alpha$_2$ agonists (via vasoconstriction).
  - – Venous return is affected by a number of factors including: circulating blood volume, body position, phase of respiration, respiratory disease (due to changes in intrathoracic pressure), and valvular regurgitation.
- o Ideally, an appropriate preload will cause the myocardium to stretch, which will improve contractility and increase stroke volume due to *Frank–Starling's Law* of the heart. (See Fig. 2.2.)

Afterload
- o Is the pressure or resistance against which the ventricle must pump in order to eject blood.
- o Although *aortic impedance* is the most accurate measurement, *arterial blood pressure* is the most commonly used index of afterload. (See section on blood pressure for more information.)
  - – Aortic impedance = Aortic pressure/Aortic flow
- o End-systolic *ventricular wall stress* is also used to describe afterload.
  - – At the end of systole, with the aortic valve open, increased resistance in the vascular system will be imposed on the ventricles and will increase ventricular wall stress.

o   Anesthetic agents that can affect afterload include *acepromazine* (vasodilation decreases afterload) and α_2 agonists (vasoconstriction increases afterload).

Contractility (inotropy)
o   Defined as the ability of cardiac muscle fibers to shorten or develop tension.
–   Cardiac muscle contraction is initiated by an action potential which triggers the release of intracellular calcium and the flux of extracellular calcium into the cell, ultimately resulting in cross-bridging of actin and myosin and a shortening of the sarcomere.
o   *Ejection fraction* is a simple measurement of contractility.
–   Ejection fraction is the ratio of the stroke volume to the end-diastolic volume.
–   Normal ejection fraction is 60–70%.
o   Other indices used to evaluate contractility include the rate of change of ventricular pressure with respect to time (dP/dt), ventricular function curves, and pressure volume loops.
o   Increased contractility causes an increase in *myocardial oxygen consumption*.
o   Factors that affect contractility include autonomic tone, acidosis, hypoxia, thyroid disorders, electrolyte imbalance and anesthetic agents.
–   Barbiturates, *propofol*, and inhalational anesthetic agents cause a decrease in myocardial contractility.
–   *Ketamine* causes an indirect increase in myocardial contractility via stimulation of the sympathetic nervous system (the direct effect of *ketamine* is to decrease contractility).

Relaxation (lusitropy)
o   Corresponds to the extrusion/reuptake of calcium and relaxation of the sarcomere.
o   Imperative for normal diastolic function.
o   Impaired by conditions like hyperthyroidism and heart failure and by anesthetic agents including most inhalational agents.

D. Blood pressure (BP)

o   Although *cardiac output* is a more precise measure of cardiovascular function, *blood pressure* is easier to measure and is often used for evaluation of the cardiovascular system. (See Chapter 14.)
o   BP = Cardiac output (Q) × Systemic vascular resistance (SVR)

$$SVR = \frac{\text{Mean arterial pressure} - \text{Mean right atrial pressure}}{\text{Cardiac output}}$$

Note: SVR is often called *total peripheral resistance* (TPR).
o   Arterial blood pressures are recorded as *systolic*, *diastolic* and *mean values*.
–   Systolic pressure = Peak pressure.
–   Diastolic pressure = Nadir pressure.
–   Mean pressure = $^1/_3$ (Systolic pressure – Diastolic pressure) + Diastolic pressure

E. Physics of flow

o   Blood in the middle of the vessel flows freely whereas it flows slowly at the periphery because of friction with the endothelium.
  – In a small vessel, a large percentage of the blood is in contact with the vessel wall so the rapidly flowing central stream is absent.
o   Blood pressure is dictated by the laws of Ohm and Poiseuille.

Ohm's Law

o   Demonstrates the relationship between current (I), resistance (R), and voltage (V) in an electrical circuit and can be expressed in three ways:

$$V = RI, \ I = \frac{V}{R}, \ or \ R = \frac{V}{I}.$$

o   It can also be used to describe blood flow (cardiac output, Q), resistance (R), and pressure differences across vessels (ΔP) in the cardiovascular system.
  – $Q = \dfrac{\Delta P}{R}$.
  – So blood flow is *directly* proportional to the pressure gradient across the vessel and *inversely* proportional to the resistance.
  – The absolute pressure in the vessel is therefore less important than the ΔP across the vessel in determining flow.

Poiseuille's Law (Hagen–Poiseuille)

o   Gives the relationship between resistance to flow and vessel dimensions and is analogous to Ohm's Law.
o   It applies to laminar flow of incompressible uniformly viscous fluids (described as 'Newtonian fluids') in uniform vessels.
  – The law does not apply to pulsatile flow.
o   Its main application is in peripheral vessels where flow is almost steady.
o   The Poiseuille equation can be derived by inserting the factors which affect resistance (R) into Ohm's Law.

$$Q = \frac{\Delta P}{R} \ and \ R = \frac{8 \eta l}{\pi r^4}$$

(for laminar blood flow in a vessel of length *l*, radius *r*, and blood viscosity η).

$$So \ with \ substitution, \ Q = \frac{\Delta P \pi r^4}{8 \eta l}.$$

o   Significance of Poiseuille's Law:
  – Because *r* in this equation is raised to the fourth power, slight changes in the vessel diameter (radius) cause tremendous changes in flow.
  – An increase in viscosity (e.g. with dehydration) will contribute to a decrease in blood flow.

Laplace's Law
- o States that for any given pressure (P), the tension (T) developed by the ventricular wall increases as the radius (R) of the cylinder increases.
    - – For a cylindrical vessel $T = P \times R$.
    - – For a spherical vessel $T = \dfrac{P \times R}{2}$.
    - – So for any given radius and internal pressure, a spherical vessel will have half the wall tension of a cylindrical vessel.
- o In the case of the heart, the left ventricle has a much greater radius than the right ventricle and thus is able to develop greater tension (or force).

Starling's Law (Frank–Starling mechanism, see Fig. 2.2)
- o Describes the intrinsic capability of the heart to increase its force of contraction in response to an increase in venous return.
    - – This response occurs in isolated hearts indicating that it is independent of humoral and neural factors.
- o *Preload* directly determines cardiac output when the heart rate is constant.
    - – An increase in preload, up to a certain point, increases cardiac output.
    - – At the end-diastolic volume, cardiac output will *not increase further* and may actually decrease.

F. Tissue oxygen delivery

- o As stated, the ultimate responsibility of the cardiovascular system is to provide adequate oxygen to the working cells.

$$\text{Tissue } O_2 \text{ delivery } (DO_2) = \text{Cardiac output } (Q) \times \text{Arterial } O_2 \text{ content } (CaO_2)$$

- o $CaO_2 = \left(\dfrac{SaO_2\%}{100} \times [Hb] \times 1.36 \right) + (PaO_2 \times 0.003)$
    - – $SaO_2 = $ per cent saturation of hemoglobin with oxygen
    - – $[Hb] = $ concentration of hemoglobin in the blood in g/dl
    - – $1.36 = $ a constant describing the amount of oxygen bound by Hb
    - – $PaO_2 = $ Partial pressure of O_2 in arterial blood
    - – $0.003 = $ the oxygen solubility constant
- o Normal $CaO_2 = (0.98 \times 15 \times 1.36) + (95 \times 0.003) = 20.28$ ml/dl,
- o CaO_2 subsequent to decreased oxygen saturation is equal to:
    $(0.85 \times 15 \times 1.36) + (85 \times 0.003) = 17.59$ ml/dl
    and CaO_2 subsequent to decreased Hb concentration is equal to:
    $(0.98 \times 6 \times 1.36) + (90 \times 0.003) = 8.27$ ml/dl
- o Thus, adequate oxygenation is important but a critical mass of circulating red cells is *imperative* for tissue oxygenation.

Table 2.1 Effects of anesthetic drugs on the cardiovascular system.

Drug	Heart rate	Heart rhythm	Pre-load	After-load	Contractility	Cardiac output
Acepromazine	↑	–	↓	↓	– or ↓	↑ or ↓
Detomidine and *xylazine*	↓↓	+	↑	↑	– or ↓	↓
Diazepam and *midazolam*	–	–	–	–	–	–
Opioids	– or ↓	–	↓	–	– or ↓	– or ↓
Thiopental	↑	+	↓	↓	↓	↓
Ketamine and *tiletamine*	↑	+	↑	↑	↑ or ↓	↑ or ↓ or –
Etomidate	–	–	–	–	–	–
Propofol	– or ↓	+	↓	↓	↓	↓
Halothane	↓	+	↓	↑	↓↓	↓
Isoflurane	↓	–	↓	↓	↓	↓
Sevoflurane	↓	–	↓	↓	↓	↓

↑ = Increased; ↓ = decreased; – = no change; + = potentially arrhythmogenic. Adapted from Muir W.W. 1998 *Compendium on Continuing Education for the Practicing Veterinarian*, **20** (1.78–87).

VII. Anesthesia

A. Effects of anesthetic agents (see Table 2.1)

- o Most drugs used for sedation/tranquillization and anesthesia cause some degree of dose-dependent cardiovascular changes which may manifest as changes in heart rate, preload, afterload, contractility or a combination of these factors.
- o Regardless of which drugs are used, drug dosages in *compromised patients* should almost always be reduced.
  - – Most side effects, like the cardiovascular depression caused by inhalational anesthetic agents, are dose-dependent.
  - – A greater percentage of administered drug may reach the brain (see below).

B. Effects of cardiovascular disease

- o Depending on the severity of the cardiovascular disease, changes in *heart rate*, *preload*, *afterload* and *contractility* can range from barely noticeable to life threatening.
- o *Decreased contractility* generally due to:
  - – Direct effects of disease (e.g. myofibril damage from ischemia).
  - – Indirect effects of electrolyte imbalance (e.g. decreased ionized calcium, acid–base imbalance, or sepsis).
- o *Increased afterload* generally due to:
  - – A hypotension-mediated increase in sympathetic activity, which results in excessive vasoconstriction in an attempt to maintain blood pressure in the face of decreased cardiac output.

- – A hypotension-mediated decrease in arterial baroreceptor inhibition of autonomic centers in the brain stem, which stimulates the release of renin, which increases vascular resistance and promotes salt and water retention through release of aldosterone.
  - o *Decreased stroke volume* due to decreased contractility and increased afterload.
    - – The decrease in *stroke volume* causes cardiac output to become more *heart-rate dependent*.
    - – Heart rate generally increases, thereby increasing myocardial O_2 consumption.
  - o *Increased preload* due to reduced stroke volume and accumulated venous return and an increase in fluid retention secondary to activation of the renin/angiotensin system.
    - – If the myofibrils can respond, this initially leads to improved contractility via the Frank–Starling law.
    - – Eventually leads to over-distension of the ventricle, which impairs contractility and increases myocardial O_2 demand.
  - o Circulation becomes 'centralized' in patients with moderate to severe cardiac disease, resulting in greater delivery of blood (and drugs carried by the blood) to highly perfused tissues, including the brain.
    - – However, cardiac output is often decreased in these patients, resulting in *slower* drug delivery to the brain.
    - – Thus, the dosage of anesthetic drugs administered to patients with cardiac disease should be *decreased* and drugs should be administered *slowly* and with ample time between doses for delivery to the brain.
  - o Congestion of blood and lack of forward flow lead to the development of *edema*.
    - – Pulmonary edema can seriously impair gas exchange.
  - o Myocardial O_2 demand increases (due to tachycardia, increased afterload, and over-distended or hypertrophic myocardium), yet O_2 supply decreases (due to decreased myocardial perfusion), possibly resulting in O_2 debt and further myocardial injury.

VIII. Cardiovascular disease in horses presented for anesthesia

A. Diseases of the conducting system

- o Include irregularities of the SA node (e.g. sinus tachycardia and vagally mediated bradycardia), the atrial conduction system (e.g. atrial fibrillation), the AV node (e.g. first-, second-, or third-degree AV block) and the bundle branch or His–Purkinje system (e.g. bundle branch block).
- o Because the equine atrial muscle mass is large, the equine heart is predisposed to the development of re-entrant rhythms such as atrial fibrillation.

Atrial fibrillation
- o *The most common pathologic arrhythmia encountered in horses.*
- o Atrial contribution to ventricular filling may be significant during anesthesia.
- o Some anesthetic drugs are arrhythmogenic and should be avoided.
- o Patients may need to be converted to normal sinus rhythm prior to anesthesia.

B. Congenital disease

- o Includes patent ductus arteriosus, ventricular septal defects and tetralogy of Fallot.

Patent ductus arteriosus (PDA)
- ○ *The most commonly encountered congenital disease in horses.*
- ○ The ductus arteriosus may be patent for up to 72 hours in normal foals.
- ○ Anesthetic-induced hypotension may reverse blood flow through the PDA and create pulmonary hypertension.

C. Primary myocardial disease

- ○ Rare in horses.
- ○ *Congestive heart failure* (CHF) is associated with limited cardiac output, increased neurohumoral activity, sodium retention, edema in tissues and transudation of fluid into body cavities.
  - – *Valvular disease* is the most common cause of CHF in the horse.
  - – Horses with congestive heart failure are at an extremely high anesthetic risk.

D. Secondary cardiovascular compromise

- ○ Common in horses presented for anesthesia.
- ○ Causes include circulatory shock (e.g. severe hemorrhage), sepsis (e.g. colic), and profound electrolyte imbalance (e.g. ruptured bladder in foals).
- ○ Cardiovascular changes that occur in sepsis include:
  - – Decreased cardiac output resulting from a direct decrease in contractility and a decrease in preload due to splanchnic pooling and vascular leakage.
  - – Pulmonary hypertension (with subsequent hypoxemia).
  - – Complex alterations in systemic blood pressure (initial hypertension followed by hypotension with loss of vascular tone).
  - – Drastic alterations in hematologic function, including hypercoagulability followed by hypocoagulability.

IX. Anesthetic plan for horses with cardiovascular disease

A. Patient preparation

- ○ All horses scheduled for anesthesia should have a thorough physical examination.
- ○ Because anesthetic drugs can drastically alter cardiovascular function, techniques to evaluate the cardiovascular system should be emphasized, especially in patients with primary cardiovascular disease or cardiovascular compromise secondary to other systemic disease (e.g. sepsis).
  - – Laboratory tests should include serum chemistry and a complete blood count.
- ○ Regardless of the cause of cardiovascular compromise, the patient must be stabilized prior to anesthesia. This includes:
  - – Restoration of circulating blood volume (use of whole blood if necessary).
  - – Intravenous fluids must be used judiciously in horses with heart failure.
  - – Restoration of electrolyte balance.
    - ■ Serum $[Ca^{2+}]$ and $[K^+]$ are often decreased.
  - – Promotion of cardiovascular function (e.g. IV fluids, positive inotropes, and analgesics).

B. Sedation and induction

○   Following stabilization, the horse should be sedated with low doses of sedatives (e.g. α_2 agonists, *acepromazine*).

○   Pre-emptive analgesic drugs should be utilized (e.g. opioids, α_2 agonists, NSAIDs), to decrease the horse's stress and the amount of induction and maintenance agents used.

○   A balanced induction technique should be used (e.g. *guaiphenesin* + *ketamine*), and low doses of the drugs should be administered to effect.

○   Intubation and oxygen administration should occur as soon as possible.

C. Maintenance

○   Inhalational anesthetics are generally used for maintenance but their concentrations should be kept as low as possible to minimize their hypotensive effects.
    – Balanced anesthesia (e.g. inhalational agent plus a *ketamine* or *lidocaine* CRI) should be considered.

○   Analgesia is imperative and can be supplied via systemic administration of drugs or by the use of local anesthetic blockade.

○   Monitoring is extremely important and should include arterial blood pressure, ECG, and arterial blood gases.
    – A cardioselective ionotrope (e.g. *dobutamine*) is recommended if indicated for blood pressure support.

○   Fluid therapy should include evaluation and support of PCV, total protein (TP), acid–base balance, and electrolyte concentrations.

D. Recovery

○   Is as critical as the other steps of anesthesia.

○   Patient support (including monitoring, fluid administration, oxygen administration, and provision of analgesia) should be maintained, when possible, throughout the recovery period.

Evaluation of the cardiovascular system

Rebecca Gompf

●   Examination of the cardiovascular system should be performed in a systematic manner. The entire horse should be examined, but particular attention should be paid to mucous membrane color and perfusion, jugular pulses, arterial pulses, percussion, and auscultation.

●   If a horse has exercise intolerance, respiratory problems, arrhythmias or heart murmurs, it should be evaluated for underlying cardiac problems.
    ○   An ECG, thoracic radiographs (depending on the size of the horse), and an echocardiogram with Doppler should be part of the minimum database for a horse with suspected heart disease.
    ○   Additional laboratory tests will help to determine the underlying cause of the problem, especially if an arrhythmia is present.

I. Cardiac examination

A. Mucous membranes (mouth or eyes)

- ○ Capillary refill time (CRT) should be < 2 seconds.
- ○ Mucous membranes (MM) should be pink.

Significance of MM color:
- ○ *Pink* and CRT < 2 seconds indicates a normal to high cardiac output.
- ○ *Bright red* with CRT < 2 seconds indicates vasodilatation with normal to low cardiac output.
- ○ *Pale pink* with CRT normal or prolonged indicates a low blood pressure and cardiac output.
- ○ *Cyanotic* with CRT normal or prolonged indicates a very low arterial pressure and cardiac output, hypoxia, and marked venous dilation.

B. Arterial pulses

- ○ Common sites for palpation are *facial*, *submaxillary*, *transverse facial* and *coccygeal* arteries.
- ○ Rate: 20–50 beats per minute.
- ○ Character: short and distinct indicates that the horse is normal or has a condition that does not affect cardiac output or peripheral vasculature resistance.

Abnormal arterial pulses
- ○ **Bradycardias** may indicate increased vagal tone, heart blocks, electrolyte problems or drug-induced effects.
- ○ **Tachycardia** may indicate fever, fear, pain, excitement, shock, heart failure, metabolic problems, drugs or other systemic diseases.
- ○ **Hypokinetic pulse** (weaker than normal pulse) is usually associated with decreased cardiac output (e.g. shock, heart failure, hypovolemia) or increased peripheral vasoconstriction (septic shock).
- ○ **Thready pulse** (weak and irregular in character) indicates heart failure, electrolyte problems, metabolic acidosis, hypovolemia, increased peripheral vasoconstriction or any combination of the above.
- ○ **Hyperkinetic pulse** (stronger than usual) is usually associated with volume overload of the heart which increases contractility (congenital heart defects) or can be due to increased sympathetic discharge.
- ○ **Pulse deficit** (the absence of an arterial pulse with each heart beat) is associated with premature beats and heart blocks.

C. Jugular pulses

- ○ With the horse standing and the head in normal position, jugular pulse will only go one-third of the way up the neck.

      ○ **Abnormal jugular pulses** are associated with:
- Right heart failure with tricuspid regurgitation.
- Heart blocks.
- Arrhythmias.
- Pulmonary hypertension.

      ○ **Distended jugular pulses** (increased venous pressures) are associated with:
- Right heart failure.
- Pericardial effusions.
- Masses obstructing venous flow.
- Pulmonary disease.

D. Percussion of the thorax

- ○ Percussion of the thorax is used to detect fluid lines.
- ○ It can also be used to tell gross enlargement of the heart and can possibly detect a large mass in the thorax.

E. Auscultation

- ○ Point of maximum intensity (PMI) is located from the third to fifth left intercostal spaces (ICS).
- ○ Displacement of PMI may indicate an enlarged heart, thoracic mass, fluid in thorax or diaphragmatic hernia.
- ○ Can sometimes perceive a murmur which is called a 'thrill'.

Valve locations
- ○ *Mitral* at fifth ICS just below the line midway between the sternum and the point of the shoulder on the left side.
- ○ *Aortic* at third ICS just below the point of the shoulder on the left side.
- ○ *Pulmonic* at third ICS below the point of the shoulder on the left side.
- ○ *Tricuspid* at third to fourth ICS on the right side at the level of the lower half of the ventral third of the thorax.

II. Normal heart sounds

- ● *First sound* (S_1) is due to closure of the mitral and tricuspid valves.
  - ○ Longer, duller, and louder at the left apex (mitral area).
- ● *Second sound* (S_2) is due to closure of the aortic and pulmonic valves.
  - ○ Short, high-pitched, and sharp.
  - ○ Loudest over the left base (pulmonic and aortic areas).
- ● *Third sound* (S_3) is due to rapid ventricular filling.
  - ○ Low pitched and soft.
  - ○ Best heard in the mitral area.
- ● *Fourth sound* (S_4) is due to atrial contraction.
  - ○ Medium in pitch.
  - ○ Best heard in the mitral area.

Heart sounds at rest
- o Split S_1 is common.
  - – Due to asynchronous closure of the mitral and tricuspid valves, especially if pulmonary disease present.
- o Split S_2 is common.
  - – Due to asynchronous closure of the aortic and pulmonic valves, especially if pulmonary hypertension is present.
- o S_1 and S_2 will always be present.
  - – May or may not be split.
- o S_3 and S_4 may or may not be present.

III. Abnormal heart sounds

- • *Gallop* rhythm is the presence of S_3 or S_4 or both when the heart rate is > 60.
  - o Usually associated with heart enlargement but can occur in a heart that has sped up due to excitement or exercise.
- • S_4, when it is heard by itself, indicates the presence of second-degree block.
- • Murmurs result from turbulent blood flow.
- • Physiology murmurs (without underlying cardiac disease) can occur in *foals*.

A. Systolic murmurs

- o Occur after S_1 and before S_2 and are associated with:
  - – Aortic or pulmonic stenosis (acquired or congenital).
  - – Tetralogy of Fallot (congenital).
  - – Mitral regurgitation and tricuspid regurgitation (acquired).
  - – Ventricular septal defects (congenital).

B. Diastolic murmurs

- o Occur after S_2 and before S_1 and are associated with:
  - – Aortic regurgitation
  - – Pulmonic regurgitation
  - – Mitral and tricuspid stenoses are *extremely rare* in horses.

C. Continuous murmurs

- o Start after S_1 and continue throughout systole and end after S_2, and are associated with:
  - – Patent ductus arteriosus (should close by 5 days of age).
  - – Arteriovenous (AV) fistulae.

IV. Electrocardiogram (ECG)

A. Components of the ECG

- ○ *P wave* represents atrial depolarization.
    - – Is usually positive in lead II and often will have an 'm' shape at rest.
- ○ *QRS* represents ventricular depolarization.
    - – Is usually positive in lead II.
    - – Is usually ≤ 1 mV in height.
    - – May or may not have all three waves present (Q, R, and S).
    - – Is always called the QRS complex.
- ○ *T wave* represents ventricular repolarization.
    - – Can be positive or negative.
- ○ *PR interval* represents time from the start of atrial depolarization (P wave) to the start of ventricular depolarization (QRS complex).
    - – Includes the time the impulse takes to go through the atrial and AV node.
- ○ *QT interval* represents from the start of the QRS complex to the end of the T wave.
    - – Includes the time of ventricular depolarization and repolarization.
- ○ *ST interval* represents the segment after the QRS complex and before the T wave.
    - – Can be very difficult to measure and so it is compared with the baseline.

B. Examination of the ECG

Ask the following three questions:

Is there a P wave for every QRS complex?
- ○ No P wave and slow rate, check for *hyperkalemia*.
- ○ No P wave and fast, irregular rate indicate *atrial fibrillation*.
- ○ No P wave and fast, regular rate and normal QRS indicate atrial or sinus tachycardia with P waves lost in the preceding QRS–T complex.
- ○ No P wave and fast rate and a wide bizarre QRS are indicative of ventricular tachycardia.

Is there a QRS for every P wave?
- ○ If there are P waves without QRS complexes, then *heart block* is present.
    - – *Second-degree* heart block (see Fig. 2.3):
        - ■ P not followed by a QRS.
        - ■ Majority of P waves have normal-appearing QRS complexes that come at a fixed distance after the P wave.

Fig. 2.3   Continuous lead II rhythm strip showing Mobitz type II second-degree heart block in a horse at rest. Notice that the PR intervals become longer and then there is a P not followed by a QRS complex.

- – *Third-degree* or complete heart block.
  - ■ No P wave is followed by QRS complexes.
  - ■ The P waves are at a regular rate and the QRS complexes are at a regular, slow rate.
  - ■ The QRS may be normal or abnormal in appearance.

Are P waves and QRS complexes associated (at a fixed PR interval)?
- o PR interval can vary slightly (≤0.04 seconds).
- o PR interval varies with normal P and QRS complexes.
  - – P waves move in and out of QRS (indicates AV dissociation).
- o PR interval varies and QRS is wide and bizarre (indicates ventricular tachycardia).

If the answers to the questions are **yes***, then the horse has a normal sinus rhythm or arrhythmia, both of which are normal in a horse at rest.*
- o *Sinus rhythm* is present when the R–R intervals do not vary by > 10%.
- o *Sinus arrhythmia* is present when the R–R intervals vary, usually with respiration.
  - – Has an increased rate (shorter R–R intervals) during inspiration and a decreased rate (longer R–R intervals) during expiration.

C. Normal rhythms at rest

- o Sinus rhythm.
- o Sinus arrhythmia.
- o Sinus arrest.
- o Sinus bradycardia.
- o Second-degree heart block.

D. Normal rhythms after exercise

- o The type of rhythm depends on the intensity of exercise.
  - – Sinus rhythm.
  - – Sinus tachycardia.

V. Arrhythmias – supraventricular

- o Only the most common supraventricular arrhythmias are discussed.
- o Arise from the atrioventricular (AV) node or above.

A. Sinus tachycardia

- o Heart rate is ≥ 50/minute with normal PQRST complexes.
- o Foals, yearlings, Draft horses, and nervous horses can have a higher heart rate and be normal.
- o Tachycardia may result from fever, pain, colic, hypovolemia, shock, infection, advanced pregnancy and heart disease/failure.

B. Premature atrial beats (PAB)

- R–R interval is shorter than normal between the normal and premature beat.
- QRS complex is the same width as the normal beat and has a similar configuration.
- Associated with:
    - Enlarged atria (check for heart disease).
    - Electrolyte problems (e.g. hypokalemia).
- Myocarditis (e.g. from toxins, infections, colic or other GI or metabolic problems).
- Single premature atrial beats may not be significant if they occur immediately post exercise, are not associated with clinical signs and are not detected during exercise (due to autonomic imbalance).

Treatment
- Not treated unless they become frequent and associated with clinical signs or the PAB triggers atrial fibrillation.
- Use *quinidine* or *digoxin* in these cases.
    - *Quinidine* to abolish the arrhythmia.
    - *Digoxin* to control it if there is underlying heart disease.

C. Atrial tachycardia

- Defined as four or more atrial premature beats in a row.
- Not a common finding in horses.
- Same causes as atrial premature beats.
- Rarely trivial and usually signifies a worsening heart condition or significant underlying problem.
- Predisposes to atrial fibrillation.
- Most often seen following treatment with *quinidine* for atrial fibrillation.
- May be sustained (continuous) or nonsustained (paroxysmal) with atrial rates of 120–300 beats per minute in sustained atrial tachycardias.
- Ventricular rates may be slower due to ectopic P waves being blocked in the AV node resulting in a slower, irregular, ventricular response rate.

D. Atrial flutter

- Rapid atrial activity seen as multiple, saw-toothed P waves (F waves) with variable AV conduction causing QRS complexes to occur irregularly and at a slower rate.
- *Uncommon* in horses.
- Same causes as atrial tachycardia.
- Treat as for *atrial fibrillation*. (See below.)

E. Atrial fibrillation (see Fig. 2.4)

- Many 'f' waves along the baseline (no P waves) with a variable QRS response.
- Rhythm is 'irregularly irregular' and the QRS complexes vary in height.
- May be associated with heart disease or can be incidental.
- Higher incidence in Standardbreds, Draft horses and Warmbloods.

Fig. 2.4   Continuous lead II rhythm strip from a 9-year-old Thoroughbred mare with atrial fibrillation. Notice the irregular R–R intervals and the absence of P waves (f waves are present).

- o If no underlying heart disease (based on echocardiogram), convert to sinus rhythm with *quinidine*.
- o There is a good conversion rate and prognosis if the heart rate is ≤ 60, the AF duration < 4 months, only soft murmurs (grade 3/6 or less) are present, and the echocardiogram shows minimal structural changes.
- o Reoccurs in 25% of cases.
- o If underlying heart disease is detected, then control the rate with *digoxin* and treat the underlying heart disease.

Treatment of AF
- o *Horses with atrial fibrillation must have a complete workup prior to being anesthetized and stabilized prior to anesthesia.*
- o If underlying heart disease, *furosemide* and *angiotension converting enzyme inhibitors* may be indicated.
- o Transvenous electroconversion has been described recently, and good success is reported with this method even in cases where the condition is relatively chronic.
- o Poor prognosis in horses with atrial fibrillation that have:
  - – Congestive heart failure (right or left sided).
  - – Increased heart rates at rest.
  - – Dilated cardiomyopathy, valvular regurgitation (mitral, tricuspid, or aortic) with heart enlargement.
  - – Atrial fibrillation of over 4 months' duration.
  - – Previous occurrence of atrial fibrillation or does *not* convert with *quinidine* therapy.

VI. Ventricular arrhythmias

- ● Only the most common ventricular arrhythmias are discussed.
- ● Arise from below the AV node.
- ● Can be caused by any systemic disease, but in the horse they are usually associated with severe diseases including:
  - o Advanced heart disease.
  - o Severe toxemia.
  - o Colic and other gastrointestinal problems.
  - o Sepsis.
  - o Electrolyte disturbances (especially K, Mg, Ca).
  - o Viral or bacterial infections.
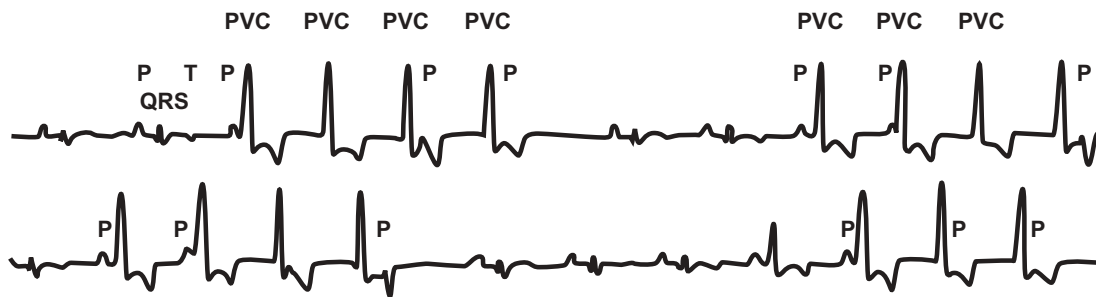
Fig. 2.5   Continuous lead II rhythm strip in a horse following abdominal surgery. Notice the wide, bizarre QRS complexes with T waves in the opposite direction which are typical of ventricular premature beats. The P waves continue to occur but are not related to the PVCs.

A. **Premature ventricular beats** (see Fig. 2.5)

- o   Premature ventricular beats or contractions (PVCs).
- o   R–R interval between the normal and abnormal beat is shorter than normal.
- o   QRS complexes are wide and bizarre with depolarization in one direction and repolarization in the opposite direction.
- o   P waves continue to occur but are not associated with the QRS complexes and many times are buried in the abnormal complexes.
- o   May be followed by a *compensatory pause* because the next impulse from the SA node is blocked by a refractory AV node.
- o   *Unifocal* means that the PVCs come from one site in the ventricle so that all the PVCs look the same.
- o   *Multifocal* means that the PVCs come from more than one site in the ventricles so that they have different appearances. This signifies more serious cardiac disease and is an indication for treatment of the PVCs.

Criteria for treatment of single PVCs
- o   Treat if PVCs are multifocal.
- o   Treat if PVCs are right on top of preceding T wave (more likely to result in ventricular fibrillation).
- o   Treat if PVCs are frequent so that the horse's pulse quality is poor.

Treatment of multiple PVCs
- o   Treat the underlying cause.
- o   Rest horses with frequent PVCs.
- o   Use *lidocaine* (0.5–1.5 mg/kg, IV) for immediate control.
- o   Use *quinidine gluconate* (1.1 to 2.2 mg/kg, IV) for short-term and *lidocaine* for long-term control (25 to 50 µg/kg/min).
  - –   Both drugs have been associated with side effects.
  - –   *Quinidine* is a negative inotrope and vagolytic; it must be used cautiously and at the correct doses.
- o   Make sure all the electrolytes (K, Mg, Ca) are normal.
  - –   Anti-arrhythmic medications are ineffective if the K or Mg concentrations are low.

B. Ventricular tachycardias

- o   The presence of four or more ventricular beats in a row.
- o   *Slow ventricular rate:*
  - –   The heart rate is just slightly higher than normal.
  - –   If the ventricular tachycardia is *unifocal*, the cardiac output may be adequate and the horse may not exhibit signs.
- o   *Fast ventricular rate:*
  - –   Not enough time for ventricular filling resulting in a decreased cardiac output.
  - –   With the PVCs coming from low in the ventricle, the ventricles contract in an abnormal sequence.

Criteria for treating ventricular tachycardia
- o   Always treat if the heart rate is >100.
  - –   Treat as for PVCs.
- o   Always treat multifocal ventricular tachycardia.
- o   Determine underlying cause.
- o   A *slow* ventricular rate does not have to be treated with drugs. The underlying cause should be determined and the horse rested for 4–8 weeks.

Drug therapy
- o   *Lidocaine* and *quinidine* (see above).
- o   If refractory:
  - –   *Procainamide* (2 mg/kg, boluses IV).
  - –   *Magnesium* (2 g bolus IV or rapid IV drip to a total of 25 g/450 kg).

VII. Bradycardias

A. Sinus bradycardia

- o   Is a slower than normal heart rate (< 26 beats per minute) with normal PQRST complexes.
- o   Usually associated with increased vagal tone and should disappear with exercise.
- o   Can be associated with:
  - –   A very fit or relaxed horse.
  - –   Increased vagal tone, either normal or secondary to GI, CNS, or respiratory problems.
  - –   Certain drugs (e.g. sedatives, anesthetics).

B. Sinoatrial arrest (sinus arrest)

- o   A long pause on the ECG longer than two normal R–R intervals.
- o   The pause may be followed by an escape beat from the AV node or ventricle.
- o   Associated with:
  - –   Increased vagal tone.
  - –   Very fit or relaxed horses.
  - –   Drugs (e.g. sedatives, anesthetics).
- o   Should disappear with exercise and does not need further therapy.

○ If it occurs during surgery and the patient is compromised, then use *atropine* or β_1 agonist (e.g. *dobutamine*).
○ After surgery, find and treat the underlying problems.

C. First-degree atrioventricular (AV) block

○ This is just an ECG diagnosis.
  – The PR interval is prolonged (> 0.44 seconds).
○ Associated with:
  – Slow heart rates: whenever the heart rate slows, the intervals on the ECG (PR, QT) will prolong.
  – Physiologic change such as increased vagal tone and drugs (e.g. *xylazine*).

D. Second-degree atrioventricular (AV) block (see Fig. 2.3)

○ A QRS complex does not follow a P wave.
○ In some horses, the fourth heart sound can be heard followed by a pause.
○ Associated with:
  – Increased vagal tone. This is a very common cause of second-degree block in horses at rest and in very fit horses.
  – Drugs: β blockers (e.g. *sotalol*), *digoxin* (toxic doses), and certain sedatives (α_2 agonists).

Treatment
○ Exercise the horse and see if the second-degree block disappears. It may require lunging the horse or riding the horse if it is fit.

Types of second-degree AV block
○ **Mobitz Type I** (Wenchebach)
  – The PR interval gradually increases until a QRS does not follow a P.
  – This is the most common type in the horse.
○ **Mobitz Type II**
  – The PR interval remains constant until a QRS complex does not follow a P.
  – This type is often coupled with disease of the AV node.

Further reading

For further and more in-depth information about all of the above topics please consult: Bonagura, JD and Reef, VB (2004) Disorders of the cardiovascular system. In: *Equine Internal Medicine*, 2nd edition, Reed, SM, Bayly, WM, Sedlum, DC (eds). W.B. Saunders Company, Philadelphia, pp. 355–460.

3 The respiratory system

Evaluation of the respiratory system

A. History

- o Should include information on the following:
  - – Nasal discharge.
  - – Coughing.
  - – Abnormal lung sounds.
  - – Increased respiratory rate and effort.

B. Physical examination

- o The rate, rhythm and character of respiration should be determined.
- o Observe the horse from all sides to assess bilateral symmetry and the thoracic and abdominal components of respiration.
- o An increase in the abdominal component of respiration may signify recurrent airway obstruction (heaves).
- o A reduced thoracic movement is a feature of acute pleuritis.
- o Assess airflow through each nostril to check the patency of the nasal passages.
  - – Closing each nostril in turn and determining airflow can verify an obstruction.
- o Abnormal odors usually signify anerobic infections (e.g. sinus, dental, lung).
- o The pharynx and larynx should be palpated externally for gross abnormalities that may affect airflow or intubation.

Auscultation
- o In adult horses, it is often difficult to hear lung sounds.
- o It may be necessary to 'amplify' the sounds by making the horse 'rebreathe' prior to auscultation.
- o Lung sounds are generally audible in the foal.

Anatomy of the respiratory system

Robert Reed

I. Organization of the respiratory system

- • The respiratory system is primarily a collection of tubular organs designed for the conduction of air and gas exchange.

- The respiratory system can be divided into:
    - The *conducting* components.
    - The *gas exchange* components.

A. Conducting components

- Consist of the nasal cavity, paranasal sinuses, pharynx, larynx, trachea, bronchi and bronchioles.

B. Gas exchange components

- The gas exchange components include the respiratory bronchioles, alveolar ducts, alveolar sacs and alveoli.

II. Tubular organs

- The tubular organs that comprise the respiratory system are made of four layers.

A. Tunica mucosa

- Contains the epithelial layer that lines the internal surface of the organ.
- The function of the organ determines the type of epithelial cells present in this layer.

B. Tunica submucosa

- The tunica submucosa is a layer of collagenous connective tissue that supports glands, blood vessels, and nervous structures.
    - The glands are responsible for secretions which moisten the epithelial surface or assist with movement of materials.
- The submucosa acts as a flexible surface onto which the tunica mucosa can attach.

C. Tunica muscularis

- Is the thickest layer of the tubular organ.
- It acts to regulate lumen size and tone.

D. Tunica adventitia

- A loose collagenous connective tissue layer that anchors organs to surrounding tissues.

III. Nasal cavity

- Each half of the nasal cavity is divided into four regions or *meatuses* by the mucous-membrane-covered dorsal and ventral *conchae*.
    - Conchae serve to warm and humidify inspired air.
    - Conchae also clean the inspired air by trapping particulate matter in mucous secretions.

IV. Paranasal sinuses

- Paranasal sinuses of the equine are found within the *frontal*, *maxillary*, *palatine* and *sphenoid* bones as well as the dorsal and ventral *conchae*.
- Paranasal sinuses are mucous-membrane-lined, air-filled cavities within bones, which serve to decrease the weight of the skull. Connections exist between the middle nasal meatuses and the paranasal sinuses that allow for increased exposure of air to mucous membrane.

V. Pharynx (see Fig. 3.1)

- The wall of the pharynx contains cartilage and skeletal muscle and is lined with a mucous membrane.
- The pharynx is subdivided into three regions (*nasopharynx*, *oropharynx* and *laryngopharynx*).
- The openings of the auditory tubes are located in the lateral walls of the nasopharynx.

Guttural pouch
- In the equine, each auditory tube has an expanded caudoventral diverticulum called the guttural pouch.
- The internal carotid arteries are closely associated with the medial compartments of the guttural pouches.
- It is believed that the air inside the pouches cools the blood within the internal carotid arteries before the blood reaches the brain.
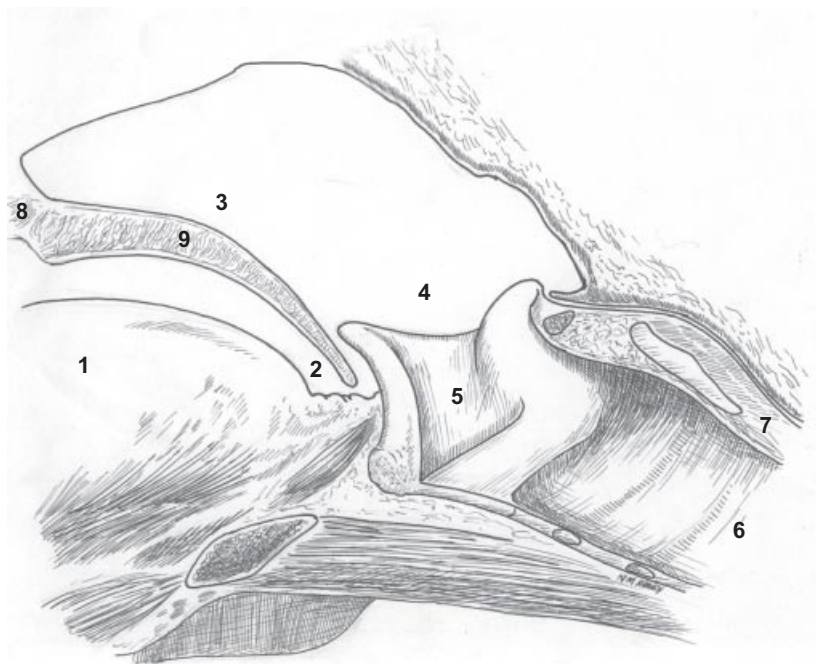
Fig. 3.1   Mid-sagittal view of equine pharynx. Tongue (1), oropharynx (2), nasopharynx (3), laryngopharynx (4), larynx (5), trachea (6), esophagus (7), hard palate (8), soft palate (9).
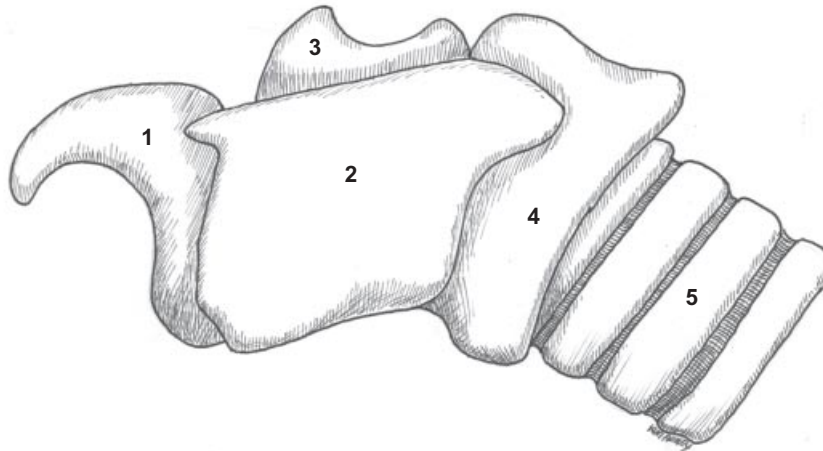
Fig. 3.2   Lateral view of equine larynx. Epiglottic cartilage (1), thyroid cartilage (2), arytenoid cartilage (3), cricoid cartilage (4), trachea (5).

VI. Larynx (see Fig. 3.2)

- Is in part composed of skeletal muscle and five individual mucous-membrane-lined cartilages.
- The opening into the larynx is called the *rima glottidis*.
- *The muscles which attach to the larynx are used for swallowing and phonation*.

A. Cartilages

- ○ *Epiglottic* cartilage functions to occlude the rima glottis during swallowing.
- ○ *Thyroid* cartilage is a trough-shaped cartilage, which forms the majority of the lateral and ventral extremities of the larynx.
- ○ *Arytenoid* cartilages (paired) are associated with the actions of the vocal ligaments and phonation.
- ○ *Cricoid* cartilage is the caudal-most cartilage of the larynx and forms a complete ring. It is responsible for maintaining patency of the larynx.

B. Innervation of the larynx

- ○ Nervous supply to the muscles of the larynx is provided by the *cranial laryngeal* and *recurrent laryngeal* nerves.
- ○ The recurrent laryngeal nerves innervate the *cricoarytenoideus dorsalis*.
  - – The cricoarytenoideus dorsalis abducts the arytenoid cartilages out of the lumen of the larynx to allow the passage of air.
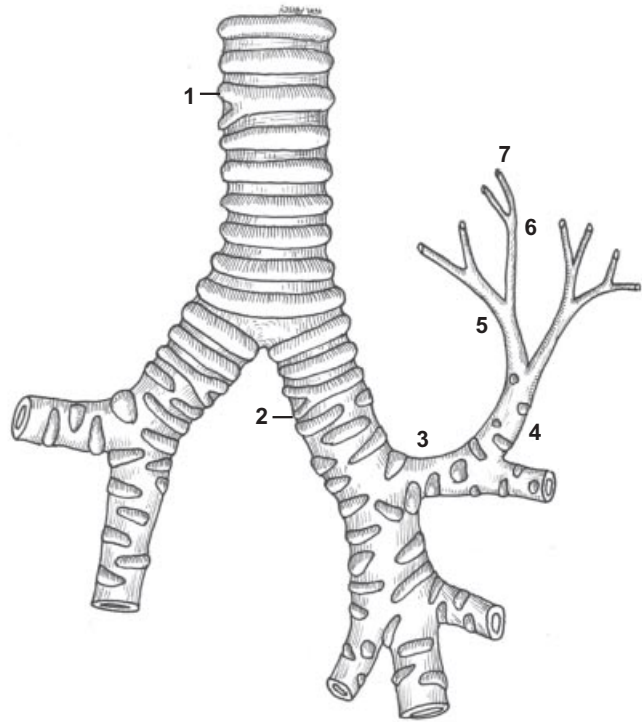
Fig. 3.3   Branching of conduction components of the respiratory system. Trachea (1), primary bronchus (2), secondary bronchus (3), tertiary bronchus (4), primary bronchiole (5), secondary bronchiole (6), tertiary bronchiole (7).

VII. Trachea (see Fig. 3.3)

- Is formed from C-shaped cartilaginous rings whose incomplete dorsal aspects are bridged by the *trachealis* muscle.
  - The trachealis muscle is composed of smooth muscle fibers.
- The tracheal cartilages prevent collapse of the trachea.
- The trachea terminates near the hilus of the lungs as it bifurcates into the left and right principal bronchi.
- The esophagus is located dorsal to the trachea in the cranial and caudal portions of the cervical region and to the left of the trachea in the middle portion of the cervical region.

VIII. Lungs and pulmonary circulation

- The lungs are a paired organ found within the thoracic cavity.
- The left and right lungs are each divided into *cranial* and *caudal lobes* by a large fissure called the *cardiac notch*.
- The right lung also possesses an *accessory lobe*.

A. Blood supply

- The lungs receive two forms of blood supply (*pulmonary*, *bronchial*).

    o The *pulmonary* circulation involves blood that is delivered to the lungs for the purpose of oxygenation.

    o The *bronchial* circulation involves blood that supplies O_2 and nutrients to the lung parenchyma.

B. Nerve supply

    o The lungs receive *sympathetic* nerve fibers from the *sympathetic trunks*.
    o The lungs receive *parasympathetic* nerve fibers from the *vagus nerves*.
    o These autonomic nerve fibers control smooth muscle and glands within the lung.

IX. Bronchi and bronchioles (see Fig. 3.3)

- Primary bronchi branch within the lung into lobar (secondary) bronchi which correspond to the lobation of the lungs.
- Secondary bronchi branch into tertiary bronchi.
- The branching of tertiary bronchi gives rise to the *bronchiolar system*.
- The bronchiolar system branches into primary, secondary and tertiary components in the same fashion as did the bronchi.
- Tertiary bronchioles give rise to *terminal bronchioles*, which are the final segment of the conducting components of the respiratory system.
- Lumen diameter of the airway decreases with each incidence of branching.

X. Respiratory epithelium

- Is the primary epithelial type lining the conducting components of the respiratory system.
- Classified as *ciliated, pseudostratified columnar epithelium with goblet cells*.
- The *goblet cells* secrete mucus which serves to trap inhaled particles.
- *Cilia* on columnar cells move this mucous layer out of the respiratory tract.
- This epithelium changes to simple columnar and eventually to simple cuboidal epithelium as the conduction system branches towards the gas exchange components.

XI. Alveolar region (see Fig. 3.4)

- Terminal bronchioles divide into several *alveolar ducts*.
- Alveolar ducts end in *alveolar sacs*.
- Alveolar sacs are dilatations of the airway lined with hemispherical chambers called *alveoli*.
- Gas exchange occurs between the blood and inspired air across the wall of the alveolus.

A. Alveoli

    o Alveoli are lined with two cell types classified as *type I* and *type II pneumonocytes*.
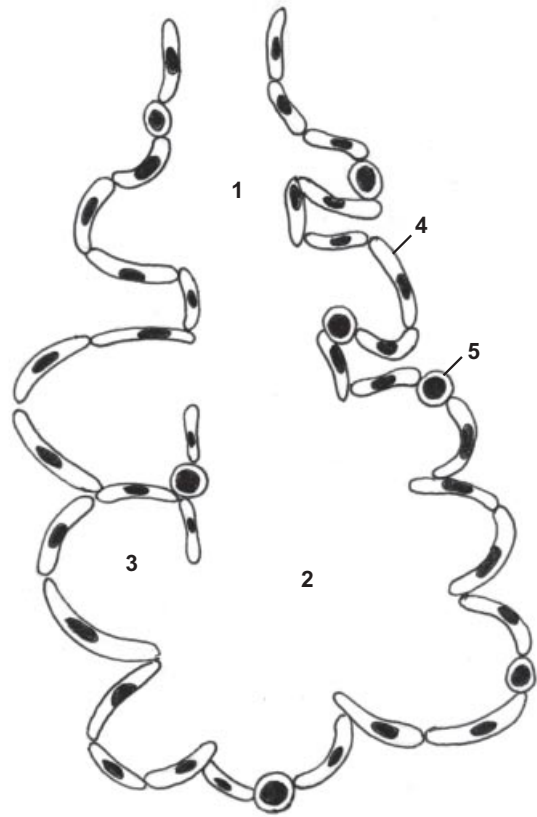
Fig. 3.4   Gas exchange components of the respiratory system. Alveolar duct (1), alveolar sac (2), alveolus (3), type I pneumonocyte (4), type II pneumonocyte (5).

B. Type I pneumonocytes

- o   Type I pneumonocytes are simple squamous cells with extremely thin processes.
- o   They are more abundant than type II pneumonocytes.
- o   They are a component of the blood–air barrier.

C. Type II pneumonocytes

- o   Type II pneumonocytes are cuboidal cells.
- o   They function to secrete *pulmonary surfactant*.
- o   Pulmonary surfactant stabilizes alveoli during inflation by keeping them uniform in size, thus preventing collapse.

XII. Blood–air barrier

- •   The partition between inspired air and the pulmonary capillary system.
- •   Formed by the processes of type I pneumonocytes, a small amount of connective tissue and capillary endothelial cells.
- •   Gas molecules must cross this barrier to enter or exit the blood vascular system.

XIII. Muscles of respiration

- The *diaphragm* is the primary muscle of respiration.
  - Innervated by the *phrenic nerves*, which originate from the fourth, fifth and sixth cervical spinal nerve pairs.
  - Contraction produces the negative pressure within the thoracic cavity involved with inspiration.
- *Scalenus*, *serratus dorsalis cranialis*, and *intercostal muscles* are also involved with inspiration.
- *Serratus dorsalis caudalis* muscles are involved with expiration.

Physiology of the respiratory system

Carolyn Kerr

- The primary function of the respiratory system is the transport of O_2 from the environment to the pulmonary capillaries and the transport of CO_2 from the pulmonary capillaries to the environment.
- Many processes are involved in achieving gas exchange. These include:
  - Ventilation.
  - Perfusion.
  - Matching of ventilation and perfusion within the lung.
  - Diffusion of gases across the alveolar capillary membrane.
  - Carriage of gases to and from the alveoli to the tissues.

I. Alveolar ventilation (V_A)

- *Ventilation* refers to the movement of gases into and out of the lung. In the normal spontaneously breathing horse, inspiration and expiration are *active* processes utilizing metabolic energy.
- Alveolar ventilation is regulated by the CNS through chemoreceptors that sense CO_2 and O_2 partial pressures in the blood, and through pulmonary reflexes and nonpulmonary neural input.

A. Mechanics of ventilation

- *Intrapleural pressure* is approximately -5 cmH$_2$O at rest, resulting in a transpulmonary pressure of 5 cmH$_2$O.
- *Inspiration* is characterized by expansion of the chest (due to contraction of the diaphragm and the external intercostal muscles), which results in a *decrease* in intrapleural pressure and an *increase* in the transpulmonary pressure gradient. As a result, gas moves from the atmosphere into the respiratory passages.
- *Gas flow* ceases at the end of inspiration, as there is no longer a gradient between the atmospheric and alveolar pressures.

o   *Expiration* is characterized by relaxation of the inspiratory muscles, elastic recoil of the lung, and contraction of the internal intercostal and abdominal muscles. These processes result in an increase in the transpulmonary pressure, and movement of gas from the lung to the ambient atmosphere.

o   *Contraction of muscles* in the nares, pharynx and larynx is necessary to prevent collapse of structures into the air passages in the presence of the negative pressures generated in the respiratory tract during inspiration. *For example, muscle relaxation secondary to the effects of sedatives or as a consequence of nerve dysfunction can impair airflow.*

B. Work of breathing

o   The work or energy expended in ventilation is due to the forces required to overcome the *elasticity* of the lung and *frictional resistance* to airflow.

o   The relative amount of energy spent on these two forces in addition to the total amount of energy spent to achieve ventilation can be altered by the *pattern of breathing*.

o   In the normal horse at rest, gas flow rate within the airways is slow, and the majority of the work of breathing is due to the *elastic resistance* of the lung.

o   As flow rates increase during more rapid respirations, a greater amount of energy is spent overcoming the frictional resistance within the airways.

C. Lung and airway resistance

o   *Elastic resistance* is a result of surface tension forces at the alveolar air–liquid interface in addition to the elastic properties of the lung tissue matrix.

o   *Frictional resistance* is primarily influenced by airway radius and length.
   –   The *upper airways* (nasal cavity, pharynx and larynx) provide approximately 60% of the total resistance to breathing.
   –   The *lower airway* resistance primarily resides in the trachea and bronchi.
   –   The *bronchioles* provide only a small fraction of the total resistance, due, in large part, to the low airflow in a high cross-sectional area.

o   *Airway radius* or diameter can be altered due to changes in the smooth muscle tone within the walls of airways.
   –   In the horse, smooth muscle extends from the trachea to the alveolar ducts.
   –   In general, parasympathetic mediated smooth muscle contraction results in airway narrowing and an increase in airway resistance.
   –   β-Adrenergic and nonadrenergic noncholinergic activation results in bronchodilation and a decrease in airway resistance.

II. Lung volumes

A. Minute ventilation (V_E)

$$V_E = f \cdot V_T$$

o   Is the total volume of air breathed each minute. It is the product of the respiratory rate (f) and the tidal volume (V_T).

o   On average, a normal adult horse breathes at a rate of 15 b.p.m. with a tidal volume of 10 ml/kg. This results in a minute ventilation of 150 ml/kg.

B. Tidal volume (V_T)

$$V_T = V_A + V_D$$

o   Each breath or tidal volume is composed of:
  –   *Alveolar ventilation* (V_A). The portion of gas that enters the respiratory zone of the lung.
  –   *Physiologic dead space* (V_D). The portion of gas that remains in the part of the respiratory system which does not participate in gas exchange.

C. Dead space

o   *Anatomical* dead space is the volume of gas that ventilates conducting airways.
o   *Alveolar* dead space is the volume of gas not taking part in effective gas exchange at the alveolar level.
o   *Physiological* dead space is the sum of anatomical and alveolar dead space.

D. Bohr equation

o   The ratio of physiologic dead space to the tidal volume (V_D/V_T) can be measured by the *Bohr equation*:

$$\frac{V_D}{V_T} = \frac{PaCO_2 - PECO_2}{PaCO_2}$$

o   This measurement is based on the fact that all expired CO_2 comes from perfused alveoli and none from dead space.
  – $PECO_2$ in this equation is the CO_2 content in the mixed expired gas, which is obtained by sampling a mixture of the expired gas collected from a large bag.
  –   In clinical practice, end-tidal CO_2 can be used to follow trends in the V_D/V_T ratio.
o   Horses have a V_D/V_T of 50–75%.
o   An increase in dead space ventilation necessitates an increase in minute ventilation in order to maintain alveolar ventilation. This results in an increase in the energy required to maintain normal gas exchange.

Factors that increase dead space
  o   Decreased pulmonary artery pressure (e.g. decreased cardiac output).
  o   Loss of perfusion to ventilated alveoli despite normal pulmonary artery pressure (e.g. pulmonary embolus).
  o   Increased airway pressure.
  o   Equipment (e.g. endotracheal tubes protruding excessively beyond the lips).
  o   Rapid, short inspirations.

Fig. 3.5   Change in lung volume with incremental changes in transpulmonary pressure generated during inflation (squares) and deflation (circles) of an equine lung. Due to the nonlinear shape of the curve, a greater change in lung volume per unit change in pressure occurs in the middle portion of the curve. In the healthy horse, FRC is located above the lower inflection point.
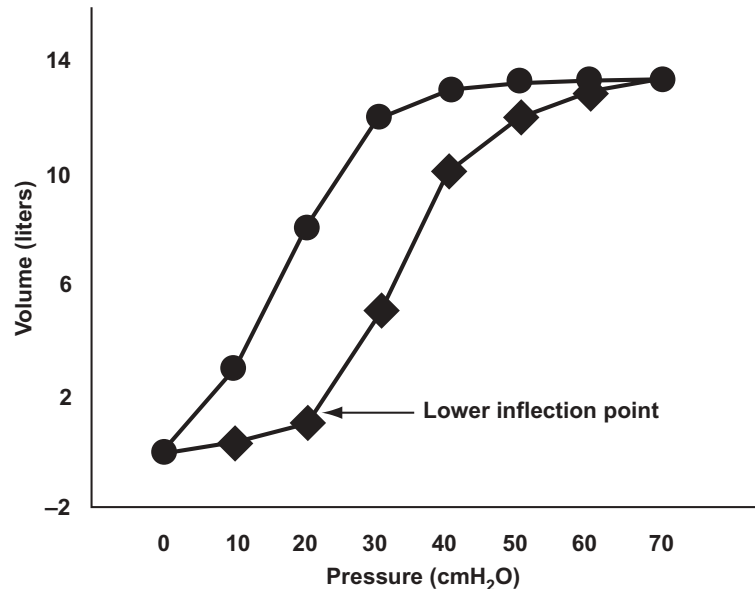
E. Functional residual capacity (FRC)

- o   At the completion of a tidal volume breath, the lung does *not empty*. The volume of gas remaining in the lung is referred to as the FRC.
- o   The volume of the FRC is important as it acts as a *reservoir* and it determines the position of the tidal volume breathing on the pressure–volume curve.
- o   If the FRC is very low, one can see from the shape of the PV curve (see Fig. 3.5) that the change in lung volume for a given change in pressure is very low.

III. Lung compliance

- •   Compliance ($\Delta V/\Delta P$) is the change in lung volume (ΔV) per unit change in transpulmonary pressure (ΔP).
- •   Pulmonary pressure–volume curves can be derived for the entire lung (see Fig. 3.5).
- •   *Compliance* is the slope of this curve and, due to the non-linear shape of the curve, it fluctuates with lung volume.
- •   In the spontaneously breathing animal with normal lungs, tidal volume breathing occurs on the steep portion of the curve. As a result, for a given change in intrapleural pressure, there is a greater change in lung volume than would occur if tidal volume breathing occurred at the extremes of the curve.

A. Distribution of alveolar ventilation

- o   The distribution of alveolar ventilation, or the change in alveolar size with each breath, is not uniform throughout the lung due to differences in the mechanical properties of the lung and chest wall.

o   In the *standing horse*, the intrapleural pressure is more sub-atmospheric in the dorsal part of the lung relative to the ventral part, due to the effect of gravity on lung tissue. The alveoli in the dorsal part of the lung are therefore more distended and less compliant than in the ventral part of the lung. As a result, alveolar ventilation per unit change in pressure is greater in the ventral compared with the dorsal part of the lung.
   –   The alveoli in the dorsal aspect of the lung would be at a location further to the right on the curve (see Fig. 3.5).

B. Factors decreasing pulmonary compliance

o   Atelectasis resulting in a loss of lung volume.
o   Pulmonary edema and/or pulmonary surfactant dysfunction.
o   Pleural, interstitial or alveolar disease.
o   Airway occlusion.
o   Pleural and/or pericardial effusion.

IV. Alveolar perfusion

A. Lung blood flow

o   The lung receives blood from two circulations, the *pulmonary artery* and the *bronchial artery*.
o   The pulmonary artery receives the total output of the right ventricle, and perfuses the alveolar capillaries.
o   The bronchial artery is a branch of the aorta and perfuses the parenchymal structures of the lung (e.g. airways).
o   The pulmonary arterial systolic, diastolic and mean pressures in the horse average 42, 18, and 22 mmHg, respectively. This indicates a *low vascular resistance* compared with the systemic circulation.
o   For gas exchange to occur across an alveolar membrane, the alveoli must be perfused. Optimal gas exchange occurs when the alveolar ventilation and blood flow are equally distributed in the lung.

B. Distribution of blood flow in lung

o   The distribution of pulmonary blood flow within the lung of the horse was previously thought to be primarily influenced by gravity; however, there is *not* a consistent vertical gradient to blood flow in the lungs of horses.
o   This implies that gravity does not play a major role in blood flow distribution.
o   *Endogenous vasoactive mediators* (e.g. nitric oxide and endothelin-1) are now thought to play a major role in the distribution of perfusion within the lung.

C. Hypoxic pulmonary vasoconstriction

o   Vasoconstriction and shunting of blood away from alveoli with low oxygen content are a result of *vasoactive mediators* acting on pulmonary vasculature.

Fig. 3.6 Diagrammatic representation of the extremes in ventilation/perfusion relationships within the lung. Optimal gas exchange occurs in lung units where the ventilation/perfusion ratio is 1. Dead-space ventilation occurs in lung units that are ventilated but not perfused, while regions that are not ventilated but are perfused result in right-to-left intrapulmonary shunt.

V/Q = 1   **Dead Space**   **Shunt**
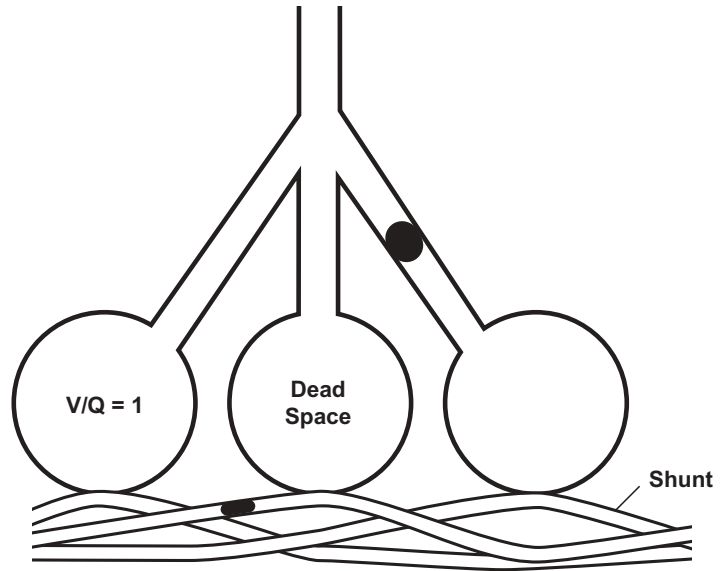
D. Ventilation/perfusion (V/Q) ratio (see Fig. 3.6)

- ○ In the normal horse, the V/Q ratio is close to 1.0.
- ○ This normal V/Q relationship may be altered by the distribution of ventilation, perfusion and/or a change in their relative distribution.
  - – When a lung unit has low or no ventilation relative to perfusion, blood leaving the unit will have lower O_2 content than units with optimal V/Q relationships.
- ○ If the V/Q relationship is 0, the blood leaving this unit will have an O_2 content similar to pulmonary artery blood.
  - – In this situation, the blood leaving this unit is referred to as an *intrapulmonary shunt* and is most commonly a result of atelectasis, partial or complete airway obstruction.
- ○ The other extreme, a V/Q ratio of infinity, is *dead space* ventilation.

V. Alveolar gas exchange

A. Composition of gases

- ○ The composition of gases in a mixture can be described by their *fractional composition* or their *partial pressures*.
- ○ The composition of gas within the alveoli is determined by the movement of gas into and out of the alveoli via the airways or across the alveolar capillary membrane and into or out of the pulmonary capillaries.

B. Movement of gases

- ○ *Bulk transfer* describes the movement of gases during inspiration and expiration within the *proximal large airways*.

    o *Diffusion* is the passive movement of gases down the concentration gradient in the *distal small airways* to the alveolus. It is the process by which gases move (i) in and out of the alveoli into the terminal airways, (ii) across the alveolar capillary membrane, and (iii) between the blood and tissues.

C. Factors influencing diffusion

    o The surface area available for diffusion.
    o The physical properties of the gas.
    o The thickness of the air–blood barrier.
    o The driving pressure of the gas between the alveolus and capillary blood as described by *Fick's law of diffusion*.

$$V_{gas} = \frac{A}{T} \cdot D \cdot (P_1 - P_2)$$

V_{gas} = the volume of gas transferred across a membrane or barrier
A = the area available for diffusion
T = the membrane thickness
D = a diffusion constant that is dependent on the physical properties of the gas.
$P_1 - P_2$ = the partial pressure difference of the gas across the membrane.

Note: CO_2 is approximately 20 times more soluble than O_2, and therefore its diffusion across a membrane is less likely to be impaired, relative to O_2, by a change in membrane thickness.

    o In the normal lung, equilibration of O_2 and CO_2 across the alveolar capillary membrane occurs within 0.25 seconds; approximately one-third of the time the blood is in the capillary.

D. Carbon dioxide

    o Carbon dioxide is the end product of aerobic metabolism. There is a continuous gradient of CO_2 from the mitochondria in peripheral cells to venous blood and then to the alveolar gas.
    o Carbon dioxide is transported in the blood in several forms including:
      – Dissolved in physical solution (~5%).
      – As carbonic acid (~90%).
      – Combined with proteins (~5%) such as carbaminohemoglobin.
    o Carbon dioxide moves from the blood to the alveoli in its dissolved form only.
    o Alveolar CO_2 partial pressures are directly proportional to CO_2 production and indirectly proportional to alveolar ventilation.

$$P_{A}CO_2 \propto \frac{V_aCO_2}{V_A}$$

Where V_aCO_2 = Rate of CO_2 production
V_A = Alveolar ventilation

o Clinically, the adequacy of alveolar ventilation is evaluated by measuring arterial CO_2 partial pressures ($PaCO_2$).
o The relationship between V_A and $PaCO_2$ is linear.
o The normal values for $PaCO_2$ and $PACO_2$ are between 35 and 45 mmHg.

E. Oxygen

o The partial pressure of oxygen in the alveoli can be determined using a simplified version of the *alveolar gas equation*:

$$PAO_2 = FiO_2(PB - PH_2O) - \frac{PaCO_2}{R}$$

FiO_2 = Fraction of inspired oxygen ≈ 0.21.
PB = Atmospheric pressure (760 mmHg at sea level).
PH_2O = Water vapour pressure (mmHg) in airway (~ 50 mmHg at body temperature of horse)
R = Respiratory gas exchange ratio (~ 0.8).

o This calculation emphasizes the significance of FiO_2 and $PaCO_2$ on the alveolar gas partial pressure.
o Clinically, this equation highlights the significance of O_2 *supplementation* for patients with impaired ventilation.

Example 1
Horse breathing room air (21% O_2) with a $PaCO_2$ = 35 mmHg:
  PAO_2 = 0.21(760 − 50) − 35/0.8 [50 = water vapour pressure (mmHg) in airway]
       = 149 − 44
  PAO_2 = 105 mmHg

Example 2
Horse breathing 100% oxygen ($PaCO_2$ = 35 mmHg):
  PAO_2 = 1.0(760 − 50) − 35/0.8
       = 710 − 44
  PAO_2 = 666 mmHg

Example 3
Anesthetized horse hypoventilating on room air ($PaCO_2$ = 70 mmHg):
  PAO_2 = 0.21(760 − 50) − 70/0.8
       = 0.21(760 − 50) − 88
  PAO_2 = 149 − 88 = 61 mmHg.
    − Although this horse is hypoxemic, a PaO_2 of < 60 mmHg is fairly typical for anesthetized horses breathing room air.
    − This example emphasizes how an increase in $PaCO_2$ affects PAO_2 and hence PaO_2.

Example 4
Anesthetized horse hypoventilating on 100% oxygen ($PaCO_2 = 70$ mmHg):

$PAO_2 = 1.0 (760 - 50) - 70/0.8$

$\quad = (760 - 50) - 88$

$PAO_2 = 710 - 88 = 622$ mmHg.

 - This example emphasizes the importance of providing O_2 during anesthesia to prevent hypoxemia.

F. Alveolar–arterial oxygen gradient [$P(A - a)O_2$]

o A small gradient in oxygen partial pressure normally exists between the alveoli (A) and the arterial blood (a).

o This gradient is due to:
 - Normal physiologic shunting of blood through bronchial and coronary veins that drain deoxygenated blood directly into the left side of the heart.
 - Normal ventilation–perfusion gradients within the lung.

o The magnitude of the gradient (A – a) can be calculated using the alveolar gas equation and by measuring the PaO_2.

o Knowledge of the magnitude of the difference in the $P(A - a)O_2$ can indicate whether a functional deficit in O_2 exchange exists.

o The significance of a calculated gradient is, however, dependent on the FiO_2.

o *Examples*:
 - In a normal horse breathing room air, the $P(A - a)O_2$ gradient is <10 mmHg.
 - A normal horse breathing 100% O_2 may have a gradient up to 70 mmHg.

o Increases in $P(A - a)O_2$ may be due to:
 - Anatomical shunting.
 - V/Q mismatching.
 - Diffusion impairment due to a thickened alveolar capillary membrane.

G. Oxygen carriage

o In blood, O_2 exists in two forms:
 - Dissolved in plasma.
 - Combined with hemoglobin.

o O_2 is poorly soluble, so the majority of O_2 in the blood is carried in combination with hemoglobin (Hb).

o *Oxygen content* of the blood (CaO_2) is calculated as the sum of the O_2 bound by Hb and that dissolved in the plasma.

$$CaO_2 (ml/dl) = \left(1.36 \times Hb(mg/dl) \times \frac{Hb\%Sat}{100} \right) + (0.003 \times PaO_2)$$

o *Oxygen delivery* to tissues (DO_2) is a function of the arterial O_2 content (CaO_2) and cardiac output.

$$DO_2 \ (ml/min) = CaO_2 \times Cardiac \ output \ (liters/min)$$
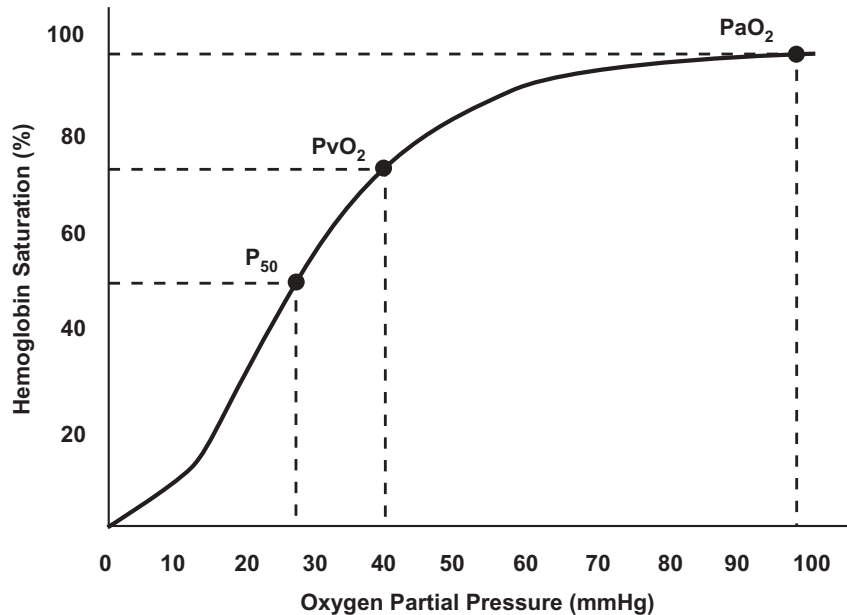
Fig. 3.7   The oxygen–hemoglobin dissociation curve showing the relationship of hemoglobin saturation to the oxygen partial pressure. The P_{50}, or the oxygen partial pressure at which hemoglobin is 50% saturated, is approximately 27 mmHg. Venous blood has a PO_2 of 40 mmHg resulting in a hemoglobin saturation of 75%. Arterial blood has a PO_2 of 98 mmHg and a hemoglobin saturation of 100%. The curve is shifted to the right with a decrease in pH or an increase in H^+, an increase in temperature, an increase in 2,3-diphosphoglycerate and/or hypercarbia. The curve shifts to the left with alkalosis or a decrease in H^+, hypothermia, low 2,3-diphosphoglycerate and/or hypocarbia.

H. Oxygen binding to Hb

- ○   Several factors can influence the binding of O_2 to hemoglobin.
- ○   The O_2–Hb dissociation curve demonstrates the relationship between PO_2 and saturation of Hb with oxygen (SO_2) (see Fig. 3.7).
  - –   A *left shift* to the curve indicates a higher affinity of Hb for O_2 and thus a higher saturation at a given PaO_2.
  - –   A *right shift* in the curve results from a lower affinity of Hb for oxygen.
- ○   The position of the curve is usually described by the position at which Hb is 50% saturated (P_{50}).
  - – P_{50} is approximately 27 mmHg in the adult horse.

I. Shunting and oxygenation

- ○   *Intrapulmonary shunts* can result in the delivery of poorly oxygenated blood into the pulmonary venous blood.
- ○   The fraction of cardiac output that passes through a shunt is expressed as the *shunt fraction* (Qs/Qt):

$$\frac{Qs}{Qt} = \frac{CcO_2 - CaO_2}{CcO_2 - CvO_2}$$

where CcO_2 = the O_2 content in pulmonary capillary blood (calculated based on PaO_2, assuming 100% saturation of Hb).
CaO_2 and CvO_2 = the O_2 content in arterial and venous blood, respectively.
In order for this calculation to be accurate, measurements must be performed when the horse is breathing 100% O_2.

- *Normal shunt fraction* is <5%.
  - Clinically insignificant shunts are 10–19%.
  - Clinically significant shunts are 20–30%.
  - Potentially *fatal* shunts are >30%.
- *Physiological shunts* are the *most common* type of shunt and they arise secondary to atelectasis or consolidation of alveoli.
- *Anatomical shunts* include bronchial, mediastinal, pleural and coronary veins.
- *Pathological anatomic* shunts include shunts secondary to congenital or traumatic anomalies and intrapulmonary tumors.
- Shunts and V/Q inequalities have a greater impact on O_2 uptake than CO_2 removal from the lungs due to the shapes of their respective dissociation curves.
  - Specifically, blood passing underventilated alveoli tends to retain its CO_2, and blood passing overventilated alveoli gives off an excessive amount of CO_2.
  - The amount of the retained CO_2 and the excessively lost CO_2 are proportional due to the relatively linear relationship of CO_2 to V_A.
  - On the other hand, blood passing underventilated alveoli does not take up enough O_2, and blood passing overventilated alveoli cannot take up a proportionately increased amount of O_2 owing to the flatness of the O_2–Hb dissociation curve in this region.

VI. Effects of sedation and anesthesia on respiratory function

A. Sedation

- In the horse, the effects of sedatives on lung function are relatively minor although differences do exist among agents.
- In general, with *acepromazine* and alpha$_2$ adrenergic agonists, ventilation changes include a *decrease in rate* and an *increase in tidal volume*.
- Alpha$_2$ agonists increase the work of breathing:
  - Due to a decrease in tone of the abductor muscles of the upper respiratory tract, thus leading to collapse of the external nares and/or laryngeal structures during inspiration.
  - The effects of increased work of breathing are insignificant in the normal horse, but may be significant in the horse with airway obstruction.
- Heavy sedation with alpha$_2$ agonists (e.g. *detomidine* 0.01 mg/kg, IV) decreases the gas exchange function of the lungs.
  - The decrease in oxygenation with detomidine sedation is due, in part, to an increase in the V/Q maldistribution within the lung.

B. General anesthesia

- ○ General anesthesia dramatically alters the function of the respiratory system.
- ○ Changes result from the *direct* effects of the anesthetic drugs on the respiratory system and the *indirect* effects of recumbency.
- ○ In the anesthetized recumbent horse, PaO_2 can markedly decrease and arterial CaO_2 and DO_2 may become critically impaired.
  - – These changes are greatest for horses in *dorsal recumbency*.
  - – Recumbency without anesthesia does not impair gas exchange to the same degree, indicating the role of the anesthetic drugs in this process.
- ○ The magnitude of the decrease in gas exchange function of the lung does not vary greatly among anesthetic protocols.

C. Mechanisms for decreased oxygenation

- ○ *V/Q mismatching* and *intrapulmonary shunting* are the major mechanisms responsible for the decrease in oxygenation during anesthesia.
  - – The distribution of ventilation changes in dorsal or lateral recumbency is due to a decrease in functional residual capacity (FRC) and regional differences in pleural pressures.
  - – Perfusion of the lungs changes due to a decrease in cardiac output, regional changes in vascular resistance, and inhibition of hypoxic pulmonary vasoconstriction.
- ○ Although the pattern of ventilation is variable among horses, in general, ventilation to the dependent regions of the lung *decreases*.
- ○ As the degree of right to left intrapulmonary shunting increases within the lung, the effect of increasing FiO_2 on PaO_2 decreases.
- ○ A decrease in arterial CO_2 removal from the lungs (e.g. with hypoventilation) with a resulting increase in $PaCO_2$ is typically observed under general anesthesia.
- ○ In general, with injectable and inhalational anesthetics, the minute ventilation and V_T are decreased, while the *f* may be increased or decreased.
- ○ The degree of respiratory depression with anesthetic agents is dose-dependent and results from drug-induced effects on the respiratory control centers.

Airway management

- Maintaining a patent airway is extremely important.
- Intubation of the trachea, via either the oral or nasal passages, requires knowledge of airway anatomy.
- It must be remembered that the horse is an *obligate nasal breather*.
- Although generally it is relatively easy to intubate the trachea of the horse, it is important to recognize situations in which airway management may be difficult.

I. Larynx

A. Function

○ The primary function of the larynx is to *protect the airway* by preventing the entry of food and foreign materials.
   – The *cricoarytenoid dorsalis muscle* is the only muscle of the larynx which abducts the arytenoids and opens the rima glottidis.
○ *Phonation* is the secondary function of the larynx.

B. Innervation

○ Motor innervation to the cricoarytenoid dorsalis is provided by the *recurrent laryngeal branch of the vagus nerve*.

C. Recurrent laryngeal neuropathy

○ Occurs primarily on the left side.
○ Is a relatively common feature in larger breed horses.
○ Results in an inability to fully abduct the arytenoid cartilage.
○ Cases of recurrent laryngeal neuropathy generally do not exhibit signs of airway embarrassment at rest.

D. Iatrogenic laryngeal neuropathy

○ Has occurred with deposition of alpha$_2$ agonists over the recurrent laryngeal nerve following accidental perivascular injection in the jugular furrow.
○ May also develop following deposition of local anesthetic in the tissues around the jugular vein.
○ This situation, while temporary, may cause severe airway obstruction necessitating passage of a nasotracheal tube or a tracheostomy.
○ Horner's syndrome may also result.

E. Hyperkalemic periodic paralysis (HYPP)

○ In foals, HYPP may cause spasm or paralysis of the pharyngeal and laryngeal muscles resulting in airflow obstruction.
   – May be accompanied by upper airway noise.
   – May observe milk discharging from the nostrils.

II. Assessment of airway

A. History

○ If intubation was difficult previously, determine if the reason has been resolved or if it was due to anatomical malformations.

B. Physical examination

- It is not possible to directly visualize the *larynx* and *pharynx* due to the shape of the horse's head and the minimal opening of the mouth. However, these structures can be assessed using an endoscope.
- Palpation of the *upper trachea* and *intermandibular space* will give an indication of swelling or increased sensitivity.
- *Pharyngeal swelling* (e.g. from abscess formation) may cause obvious signs of airway obstruction.
- *Guttural pouch tympany* in foals may result in distortion of the pharynx.
- Dysphagia resulting from *swelling of the tongue* or *pharynx* may indicate a difficult intubation.
- In cases of *mandibular fracture*, use of a mouth gag may be contraindicated and nasal intubation may be necessary.
  - If nasal intubation is to be performed, determine if the nasal passages are patent by assessing *airflow at the nostrils*.

C. Situations in which difficulty is to be expected

Recurrent laryngeal neuropathy
- To prevent damage to the adducted arytenoid cartilage it is usually necessary to use a slightly smaller-sized endotracheal tube.
  - A smaller tube will also facilitate the surgical approach and may obviate removal of the tube, intraoperatively, for surgical assessment.

Pharyngeal abscessation and lymphadenopathy
- May cause misalignment of oral, laryngeal and pharyngeal structures.

III. Airway equipment

- While it may be considered ideal to intubate the airway at all times in the anesthetized horse, it is *not* routinely practiced under field conditions.
- Airway obstruction is uncommon in the nonintubated horse during short procedures.

A. Mouth gag

- Necessary to keep the jaws open and allow passage of an endotracheal tube.
  - However, there is generally no need to use a gag in neonatal foals.
- The gag is fitted between the upper and lower incisors and care must be taken to avoid pressure on the hard palate.
- A variety of gags may be purchased from commercial vendors, or a gag may be fashioned from a piece of PVC pipe.
  - PVC gags are lightweight and unobtrusive.

B. Laryngoscope

- Not used in the horse, as direct visualization of the larynx is not possible with this method.

C. **Endotracheal tubes**

o Most endotracheal tubes are made from non-toxic plastic or silicone and are numbered according to their internal diameter (mm).
o Tube selection is generally based on the body mass of the horse.
   – Most adult, full-size horses (400–500 kg) require a tube size of 26 mm.
   – Larger horses (≥ 500 kg) require a tube of 30 mm or greater.
   – The airway of the newborn foal (40–50 kg) should accommodate a tube diameter of 10–11 mm.
   – A newborn mini breed (~10 kg) will need a smaller diameter tube (6–7 mm).
o There is generally little danger of bronchial intubation.

D. **Inflatable cuffs**

o Inflation of the cuff creates a seal with the tracheal mucosa.
o This allows the airway to be inflated under positive pressure and protects the lungs from aspiration of foreign material (e.g. gastric contents).
o It is important not to overinflate the cuff (see Section IV-C).

IV. Complications of airway intubation

A. **Tissue damage**

o To avoid tissue damage, it is important that a gentle technique be employed.
o Even the seemingly most gentle intubation can cause bruising of the tissues of the pharynx, larynx, and trachea.
o A rough technique may result in impaction of the epiglottis into the rima glottidis.

B. **Edema**

o May result from persistent attempts to pass the tube.
o Causes narrowing of the glottis.

C. **Overinflation of the cuff**

o An increase in cuff pressure will be transferred to the capillaries in the tracheal mucosa and may occlude flow.
   – Arteriolar capillary pressure is ~ 30 mmHg, and during ventilation of adult horses cuff pressures of ~ 60–70 mmHg are necessary to prevent leaks.
o Ischemia may result in necrosis of the airway mucosa.
o Selection of a suitably sized tube will prevent having to overinflate the cuff to create a seal.
o Checking the cuff pressure with a *manometer* will prevent overinflation.

D. **Lubrication**

o Lubrication of the tube with water or a water-soluble gel will facilitate its passage.
o It is especially important that a lubricant gel be used liberally for *nasotracheal* intubation.

V. Intubation of trachea

A. Difficulty

- o Horses are relatively easy to intubate due, in part, to the poor reflex responses of the larynx.
- o Flushing the mouth with water prior to induction prevents food materials from being pushed into the airway.
- o Foals often have straw or shavings from the bedding in their mouths and these should be removed.

B. Position

- o Intubation is usually performed with the horse in *lateral recumbency*.
- o If there is a likelihood of reflux of gastric contents, the horse should be kept *sternal* until the tube is inserted and the cuff inflated.

C. Technique

- o Intubation is accomplished blindly.
- o The head and neck should be extended and the tube advanced into the mouth towards the pharynx.
  - – Avoid rubbing the dependent eye on the ground.
- o At this location, the tube may touch the underside of the epiglottic cartilage which must now be dislodged from its position dorsal to the soft palate.
- o Withdrawing the tube slightly and rotating it will usually reposition the epiglottis and allow the tube to advance. If not, repeat the procedure until successful.
- o *Avoid the temptation to force the tube forward*.

D. Confirmation of tracheal tube placement

- o The tube will advance easily (unless it is too large) if in the trachea. If the trachea is held gently in the free hand, the movement of the tube along the trachal rings can be perceived.
- o If apnea is present, a gentle compression on the thoracic wall will force air out through a correctly placed tube.
- o Esophageal placement of the tube is easily detected, as the tube doesn't move easily and will recoil slightly if the driving hand is removed.
  - – The esophagus is a 'potential space' and will not be dilated in the normal state.

E. Intubation of the difficult airway

- o In rare situations, when a horse has signs of distress due to airway obstruction, it may be necessary to perform a *tracheostomy* and insert an endotracheal tube prior to sedation.
- o In the majority of these cases, the passage of an orotracheal tube can be greatly facilitated by using a narrow-bore tube (e.g. stomach tube) as a guide.
- o A suitably sized stomach tube is inserted through the lumen of the endotracheal tube and passed through the oropharynx into the larynx and proximal trachea, and this serves as a guide for passage of the endotracheal tube.

VI. Extubation of trachea

- *Spontaneous breathing* should have resumed before the tube is removed.
- Confirm that the horse is taking regular deep breaths.
- Removal of the tube before the horse has regained the swallowing reflex is generally acceptable, but many advocate waiting until this reflex has returned.
- It is also acceptable to leave an orotracheal or nasotracheal tube in place during recovery and this may be indicated under certain circumstances.
- Horses tolerate orotracheal and nasotracheal tubes well.
- Since the horse does not produce significant salivary secretions, it is not necessary to drain or suction the oropharynx prior to tube removal.

VII. Airway obstruction

- *The importance of preventing airway obstruction cannot be overemphasized.*
- Obstruction in the recovery phase will lead to extreme anxiety in the awakening horse such that it may be impossible to control the horse to establish an airway.
- Thus, it is important to check for airway patency following endotracheal tube removal.
  - This can be done by placing a hand close to the horse's nostrils and checking for airflow, while at the same time observing thoraco-abdominal excursion.
- Routine placement of a *nasal tube* following extubation will greatly reduce the incidence of airway obstruction.

A. Signs of obstruction

- Snoring sounds.
- No evidence of air passage via nostrils (hold palm of hand over nostril).
- Increased abdominal effort on inspiration and expiration.
- Abnormal abdominal movements (e.g. retraction of abdomen on inspiration).
- Nostril flaring on inspiration.

B. Laryngospasm

- Defined as reflex closure of the vocal cords.
- Does not seem to occur in the horse.
- Indeed, the larynx of the horse is much less sensitive than that of other species.

C. Obstruction of upper airway

At induction
- Obstruction is a rare occurrence, unless there is a space-occupying mass in the pharynx or the horse has severe recurrent laryngeal neuropathy.
- However, overzealous attempts to intubate may cause a partial obstruction either by causing edema or by displacing the epiglottis.
- *Treatment* – passing a narrow-bore tube (see Section V(E)) to serve as a guide for the endotracheal tube is usually successful.

At extubation
- o   The horse must suddenly change from being a *mouth breather* to having to resume *nasal breathing*, so obstruction of the upper airway is more likely to occur following extubation, especially if the horse is still deeply anesthetized.
- o   The epiglottis needs to be realigned to its normal position, dorsal to the soft palate, for successful nasal breathing to resume.
- o   HYPP may result in airway obstruction at extubation.
  - –   Usually accompanied by other signs (e.g. muscle fasciculations, prolonged recovery).
- o   *Treatment* – gentle passage of a small-bore nasal tube into the pharynx may realign the epiglottis.

Intraoperatively
- o   Obstruction is an uncommon occurrence in the intubated horse.
- o   However, extreme flexion of the neck may result in kinking and obstruction of the endotracheal tube.
  - –   The most likely scenario for this occurrence is during radiographic imaging of the cervical vertebrae, during which extreme flexion of the neck is employed.

D. Obstruction of nasal passages due to edema

- o   Is a common occurrence, especially following a prolonged period of anesthesia with the horse in dorsal recumbency.
- o   Edema develops because of the increased hydrostatic pressure in the nasal mucosa in dorsal recumbency.
- o   Passage of a nasotracheal tube is usually effective in the treatment of nasal obstruction.
  - –   A 16–18 mm tube will suffice for an adult and should be left in place for recovery.
  - –   Routine use of a nasal tube in recovery is recommended following long surgeries, especially if the horse has been in dorsal recumbency.
- o   *Phenylephrine* instillation, to constrict nasal mucosa, can be used to reduce edema.
  - –   Phenylephrine can be squirted into the nasal passages via the ventral meatus by elevating the nose and allowing contact with the nasal mucosa.
  - –   5 ml of 0.15% phenylephrine (adult, full-sized horse) into each nostril, about 30 minutes before extubation, will reduce nasal edema.
  - –   The dose should be reduced proportionally in foals and smaller horses to prevent extreme hypertension.

E. Obstruction of nasal passages due to nasal bleeding

- o   Bleeding upon removal of a nasotracheal or stomach tube can be quite alarming.
- o   *It may be best to leave nasotracheal tubes in place until the horse is standing*.
- o   The horse's head must be tilted downward to prevent aspiration of blood.
- o   It may be necessary to pass a nasotracheal tube down the unaffected nostril to protect the airway.
  - –   This can be difficult unless the horse is in a relatively deep plane of anesthesia.
- o   Some cases necessitate deepening anesthesia to facilitate re-intubation and to prevent the horse awakening until the hemorrhage has ceased.

F. Pulmonary edema as a consequence of airway obstruction

- Has been reported in horses during recovery.
- Can be fatal.

Clinical signs
- Exaggerated inspiratory effort.
- Tachypnea and tachycardia.
- Cyanosis of mucous membranes.
- Presence of blood-tinged frothy fluid in endotracheal tube or from nostrils in the postobstruction period.

Proposed pathogenesis
- In attempting to inhale forcibly against an obstruction, the horse generates an exceedingly high negative intrathoracic pressure with a resultant increase in venous return to the heart.
- However, cardiac output is decreased due to a decrease in pulmonary drainage into the left atrium.
- The process is exacerbated by hypoxia and the resulting hyperadrenergic state.
- The ensuing increase in pulmonary capillary pressure results in alveolar fluid accumulation.

Treatment
- Remove obstruction.
- Provide an airway and O_2.
- Administer diuretics (e.g. *furosemide*).
- Administer corticosteroids.

Temporary tracheostomy

Frederik Pauwels

I. Indications

A. Mechanical obstruction of the upper airway

- Nasal septal deformities.
- Space-occupying lesions (tumors, abscessed lymph nodes, fractured bony structures of the nasal cavity).
- Bilateral, postanesthetic nasal or laryngeal edema.
- Bilateral, postanesthetic recurrent laryngeal neuropathy.
- Smoke inhalation injury.
- Snake bite to the face.

B. Prophylactic

- Surgery of the upper airway that could induce upper airway obstruction, such as resection of the nasal septum.

     ○   Surgery that requires exposure of the lumen of the larynx or oropharynx, such as arytenoidectomy and cleft palate repair.

II. Surgical anatomy

- The *trachea* lies most superficially at the junction of the proximal and middle thirds of the ventral aspect of the neck.
- At this site, it is covered only by:
    - ○ The paired *sternothyrohyoideus* muscles.
    - ○ The *cutaneous colli* muscle.
    - ○ The skin.
- This site approximates the third to fifth tracheal rings.
- The paired *omohyoideus* muscles cover the trachea proximal to this site.
- The *vagosympathetic trunk*, *recurrent laryngeal nerves* and the *common carotid artery* are located dorsolateral to the trachea at this site.

III. Materials

- Clippers, surgical scrub, sterile gloves, surgical blade and handle, local anesthetic (e.g. *lidocaine*, *mepivacaine*), sedative (e.g. *xylazine*) syringes, and needles.
- Types of tracheostomy tubes (see Fig. 3.8).

Fig. 3.8 Types of temporary tracheostomy tubes.
(A) Bivona flexible tracheostomy tube with inflatable cuff;
(B) metal tracheostomy tube;
(C) Pape's tracheostomy tube;
(D) tracheostomy tube fashioned from a plastic gallon-jug handle.
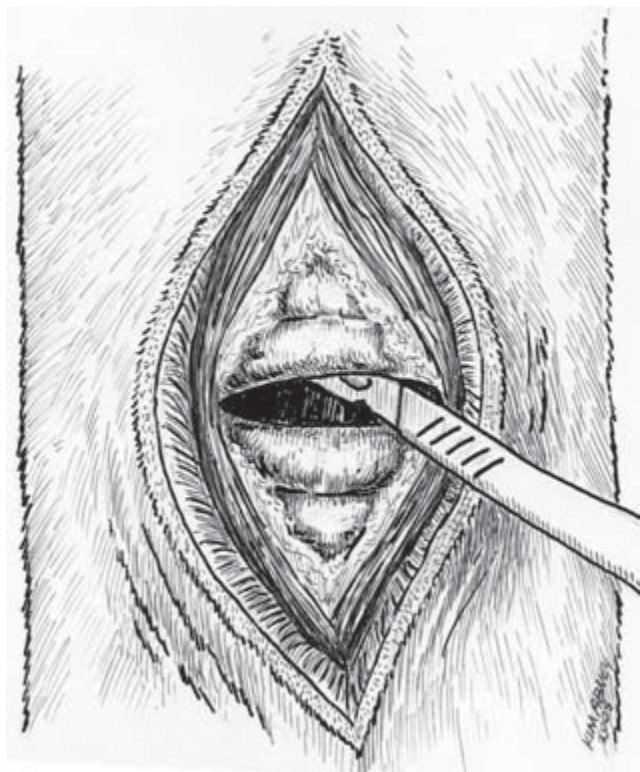
Fig. 3.9   The surgical approach for a temporary tracheostomy.

IV. Technique (see Fig. 3.9)

- Sedate the horse lightly.
- Clip and prepare 20-cm-long rectangular site, centered over the junction of the proximal and middle thirds of the ventral aspect of the neck.
- Infiltrate subcutis and deeper tissue with a local anesthetic over a 10-cm-long area on the ventral midline.
- Incise skin and subcutis longitudinally over 10 cm.
- Do *not* elevate the head too high or move the skin laterally.
- Performing a tracheostomy with the horse in lateral recumbency can cause the skin to move laterally, predisposing to displacement of the tracheostomy tube when the horse resumes a natural position.
    - The paired sternothyrohyoideus muscles are separated on midline, using a combination of sharp and blunt dissection, to expose the trachea.
    - The annular ligament lowest in the incision is incised for *no more* than 180° of the circumference of the trachea.
    - Positioning the tracheostomy in the lower half of the incision allows for more free movement of the skin when the horse lowers its neck.
    - Incising more than 180° may predispose to tracheal stenosis after the tracheostomy tube is removed and may risk damage to the carotid arteries or recurrent laryngeal nerves.

- When performing a tracheostomy on a *small horse* or a *foal*, care needs to be taken not to incise the dorsal aspect of the mucosa or even to transect the trachea.
  - Severing a cartilage ring may result in enfolding of the cut edges of the ring into the tracheal lumen.
- *Separate the tracheal rings* using the fingers for tracheostomy tube insertion.
  - Alternatively, the rings can be separated with a suture placed around the ventral aspect of the tracheal ring proximal to the tracheal incision and a similar suture placed around the ventral aspect of the tracheal ring distal to the incision.
  - These sutures facilitate removal and re-insertion of the tube for cleaning and prevent the tube from being inserted submucosally or in the loose areolar tissue ventral to the trachea.
- The tube is secured with a gauze bandage wrapped around the neck, unless it is a self-retaining tube.
  - The tube can also be secured with sutures or with elastic adhesive tape.
- *Do not* suture the skin incision around the tracheostomy tube.
  - Closing the skin incision predisposes to infection and aggravates emphysema, which inevitably develops around the tracheostomy site.

V. Postoperative care

- Administer tetanus prophylaxis.
- Administer antimicrobials until granulation tissue covers the wound edge.
- Secretions quickly clog the tracheostomy tube, and so the tube must be cleaned regularly.
  - Clean three or four times daily the first few days and thereafter once daily.
  - The tube *must* be removed for cleaning.
  - A second, clean tracheostomy tube can be inserted during cleaning.
- Petroleum jelly is applied to the site of tracheostomy to prevent scalding.
- Temporary tracheostomy tubes can be maintained in the trachea indefinitely.
- Granulation tissue develops around the tube within 4–5 days and closes the tracheostomy site rapidly after the tracheostomy tube is removed.

VI. Emergency tracheostomy

- May not be time for clipping, surgical preparation, and local anesthesia.
- A longitudinal incision is made down to the trachea at the junction of the proximal and middle thirds of the ventral aspect of the neck.
- The annular ligament between two tracheal rings is incised to the degree necessary to insert a tracheostomy tube.
- The tracheostomy can be held patent with fingers until a tracheostomy tube is found or a suitable temporary tracheostomy tube is made.
  - A temporary tracheostomy tube can be made from the cut end of a large stomach tube, the sawn-off barrel of a 30- or 60 ml syringe with holes made through the sides to attach a gauze bandage, or the handle of a 5-gallon plastic jug, which can be cut to a similar shape as a commercially available J-tube.
- If the horse cannot be controlled, waiting until it becomes recumbent may be necessary so that the tracheostomy can be performed safely.

VII. Complications

- *Infection* which can migrate along fascial planes and cause mediastinitis.
- *Severe subcutaneous emphysema* (some emphysema is inevitable).
- *Airway obstruction* due to exuberant granulation tissue, cicatrix formation, or cartilage proliferation.
- *Pneumothorax* due to emphysema migrating along fascial planes.

Ventilation of the horse with recurrent airway obstruction

Carolyn Kerr

I. Changes in lung function

- Horses with recurrent airway obstruction have an increased frictional resistance to breathing as a result of bronchoconstriction and the presence of excessive airway secretions.
- In severe cases, V/Q mismatching, an increase in minute ventilation, and hypoxemia may be present.
- Due to V/Q mismatching, there will be a wide variation in time constants.
- There is likely to be a reduced CNS sensitivity to normal and subnormal fluctuations in pH and PaO_2.
  - Thus, horses with recurrent airway obstruction can be expected to have inadequate responses to hypoxemia or acidemia in the perioperative period.
- To compensate for airway narrowing, the functional residual capacity (FRC) increases.
  - The increased radial traction, consequent to the increase in FRC, may result in airway dilation and a decrease in resistance.

II. Anesthesia of horses with recurrent airway obstruction

- Stabilization of the clinical signs prior to anesthesia is preferable.
- In the *emergency situation* and when anesthetizing the severely affected horse, the anesthetist should be prepared to supplement O_2 and support ventilation.
- During controlled ventilation, a longer *inspiratory* time (3 seconds for adult horses) is recommended due to the wide variation in ventilation/perfusion time constants.
- It is also important to allow adequate time for the *expiratory phase* as expiration is impaired by the combination of defective elastic recoil and airway closure.
- *Albuterol* (aerosolized at 2 µg/kg) may be beneficial during anesthesia.

4 The renal system

Ben Buchanan

Anesthesia and the renal system

- The equine kidney receives 15–20% of the cardiac output at rest.
- Twenty per cent of the blood entering the glomeruli is filtered through Bowman's capsule.
  - This is equal to 1200–1400 liters/day for a 500 kg horse.
- This volume greatly exceeds the 10 liters of the urine produced daily, indicating that up to 99% of the filtrate is reabsorbed.
- These activities account for 10% of the body's oxygen utilization.
  - Up to 80% of renal O_2 consumption is used for sodium reabsorption.
- This high oxygen demand makes the kidney tubules susceptible to *hypoxic damage* as may occur with a decrease in perfusion during anesthesia.

I. Role of the kidney

- The kidneys are responsible for:
  - Elimination of nitrogenous and organic waste.
  - Regulation of body water and electrolytes.
  - Maintenance of acid–base status.

II. Urine formation

A. Control of urine formation

- Urine formation is controlled by neurohormonal and physiologic factors which regulate sodium and water reabsorption.
- These controlling factors include *aldosterone*, *arginine vasopressin*, *renin*, *angiotensin II*, *atrial natriuretic peptide*, *prostaglandins*, *catecholamines*, *arterial blood pressure* and *stress*.

B. Glomerular filtration

- Filtration is performed in the glomerulus and the rate is determined by:
  - Renal blood flow.
  - Neural and hormonal influences.
  - Intrarenal autoregulation.
  - Plasma oncotic pressure.

C. Tubular function

- ○ Solute reabsorption.
- ○ Solute secretion.
  - – These processes are influenced by hormonal and neural factors.
  - – Factors increasing sodium excretion increase urine volume.
  - – Urine osmolality (concentration) is influenced by arginine vasopressin in the collecting ducts.

III. Effects of anesthetics on renal function

- ● Anesthetics affect many aspects of renal function. Virtually all anesthetic drugs have direct and indirect effects to modulate renal blood flow (RBF) and glomerular flow rate (GFR).
  - ○ Glomerular filtration rate is decreased.
  - ○ The ability to excrete sodium is reduced.
    - – This is thought to be a result of inhibition of Na^+/K^+ ATPase.
  - ○ Urine volume is affected. (See below.)
- ● A number of factors are involved in initiating anesthetic-induced changes in renal function, and the contribution of each factor is primarily dependent on the horse's physiological state and the anesthetic regimen. Factors include:
  - ○ Decreases in cardiac output and arterial blood pressure.
  - ○ Increases in sympathetic outflow from renal nerves.
  - ○ Activation of the renin–angiotensin system.
  - ○ Increased release of vasopressin.
  - ○ Direct renal effects of anesthetics.

A. Changes in renal blood flow with anesthetics

- ○ May partially result from the systemic changes invoked by anesthetics.
- ○ A redistribution of cardiac output occurs with an increase in flow to the vessel-rich areas (e.g. brain) and a reduction of flow to the splanchnic system.
- ○ The effect of anesthetics on autoregulation and intrarenal blood flow is specific to the drug in question and depends on renal perfusion pressure.
- ○ $Alpha_1$ receptors are numerous in the renal vasculature and modulate RBF by mediating vasoconstriction.

B. Inhaled anesthetics

- ○ Most inhalational anesthetics have dose-dependent effects on renal function.
- ○ In general, RBF is decreased.
- ○ All inhalational anesthetics decrease GFR.
- ○ Renal vascular resistance increases with most anesthetics.

Nephrotoxicity
- ○ Mainly a problem with 'older' inhalational drugs (e.g. *methoxyflurane*, *enflurane*).

- o *Methoxyflurane* undergoes extensive biotransformation (~50%) producing free fluoride ion and oxalate.
    – Prolonged administration results in polyuric renal failure.
    – NSAIDs potentiate the nephrotoxicity of inhalants.
- o *Sevoflurane* undergoes biotransformation (~5%) and forms fluoride ions.
    – CO_2 absorbents react with *sevoflurane* to form compound A, a vinyl ether.
    – Compound A causes nephrotoxicity in rats following prolonged exposure.
    – The amount of compound A formed is regulated by the concentration of the cysteine conjugate β-lyase, which transforms cysteine conjugates into toxic products.
    – The pathway of compound A metabolism has not been described for the horse. In any case, compound A is unlikely to be a cause of renal failure.
- o *Halothane* undergoes reaction with soda lime, but renal failure does not seem to be a clinical concern.

C. Alpha₂ agonists

- o Little effect on RBF or GFR.
- o Diuresis results from:
    – A reduced effect of vasopressin on the distal tubule and collecting duct.
    – Increased release of atrial natriuretic peptide (ANP).

D. Other injectable sedatives and anesthetics

- o Most drugs are metabolized in the liver and excreted to some extent by the renal system.
- o Renal dysfunction may, in theory, prolong the effects of anesthetic drugs but is rarely clinically significant.

IV. Diuretics

- o Diuretics have many different mechanisms of action which lead to increased urine production.

A. Osmotic diuretics

- o Are filtered through the glomerulus and increase osmotic pressure in tubule. This reduces transmembrane water flow.
- o Affects proximal tubule and collecting ducts.
- o Example: *mannitol*.
  Note: Glucosuria will also induce osmotic diuresis.

B. Carbonic anhydrase inhibitors

- o Decrease sodium reabsorption and hydrogen secretion.
- o Inhibit luminal carbonic anhydrase mainly in the proximal tubule.
- o Example: *acetazolamide* (used to treat HYPP cases prior to surgery).

C. **Thiazides**

○ Inhibit Na^+/Cl^- co-transport in the distal convoluted tubule.
○ Rarely used in horses.

D. **Loop diuretics** (e.g. *furosemide*)

○ Most commonly used diuretic.
○ Inhibit Na^+/Cl^- co-transport in the thick portion of the ascending limb of loop of Henle.
○ Bind specifically and reversibly to the chloride ion binding site of the transporter that regulates the coupled entry of Na^+/K^+/Cl^-.
○ Blocks the ability of kidney to develop counter-current mechanism limiting the ability to concentrate or dilute urine.
○ Diuretic effects are blocked by NSAIDs.
○ Potentiate toxicity of aminoglycosides.

E. **Potassium-sparing diuretics**

○ Aldosterone inhibitors (e.g. *spironolactone*)
  – Block effects of aldosterone leading to reduced sodium reabsorption
  – Affect distal tubule and collecting duct.
○ Sodium channel blockers (e.g. *amiloride*)
  – Filtered and secreted in proximal tubule.
  – Blocks movement of sodium into cells, reducing its reabsorption.
  – Affects distal tubule and collecting ducts.

V. Nonsteroidal anti-inflammatory drugs (NSAIDs)

● Can cause tubular damage especially during pathologic states or during decreased renal perfusion.
● Inhibit prostaglandin production in kidney.
  ○ Prostaglandins have an important role in vasomotor control in the kidney.
● May limit ability to increase renal blood flow to counteract vasoconstrictive effects of sympathetic stimulation or angiotensin II during times of hypotension.
● Prostaglandin synthesis in the kidney is stimulated by angiotensin II, stress, and sympathetic stimulation.
● Prostaglandin-mediated autoregulation protects the kidney until the mean arterial pressure falls below 70 mmHg.
● Reduced perfusion causes renal ischemia and tubular damage.

5 Neurophysiology and neuroanesthesia

Tanya Duke

Neuroanesthesia

- Although the requirement of anesthesia for horses with intracranial pathology is rare, an understanding of the effects of anesthetic drugs on pathophysiological processes is important in the event that general anesthesia may be required.
- Horses with seizures may be anesthetized for diagnostic procedures or for control of seizures.

I. Neurophysiology

A. Membrane potentials

- o Membrane potentials are maintained through differential distribution of ions across the nerve cell membrane.
- o Depolarization allows movement of sodium and potassium ions, which can act to depolarize the next segment of the nerve cell. This allows transmission of impulses along nerve axons.

B. Synaptic transmission

- o Junctions between nerve cells allow nerve transmission to take multiple pathways.
- o Excitatory or inhibitory neurotransmitters are released into the synaptic cleft to activate receptor sites on the post-synaptic cell.
- o Excitatory neurotransmitters in the CNS include acetylcholine, norepinephrine, dopamine, 5-hydroxytryptamine, Substance P, glutamate, and other amino acids.
- o Inhibitory neurotransmitters include glycine, GABA, enkephalins, and endorphins.
- o Other transmitters include neurotensin, thyrotropin releasing hormone, gonadotrophin releasing hormone, melanocyte stimulating releasing-inhibitory factor, adrenocorticotropic hormone, and somatostatin.

C. Brain metabolism

- o The brain uses glucose almost exclusively as a source of energy. The brain can also use two ketones, 3-hydroxybutyrate and acetoacetate.
- o The selectivity of the blood–brain barrier makes the brain dependent on glucose as an energy substrate, and low concentrations decrease the level of consciousness.
- o Twenty-five per cent of glucose is used for energy, and the remainder is used for protein synthesis (e.g. glutamic and aspartic acid) which are also used for energy in some cell pathways.
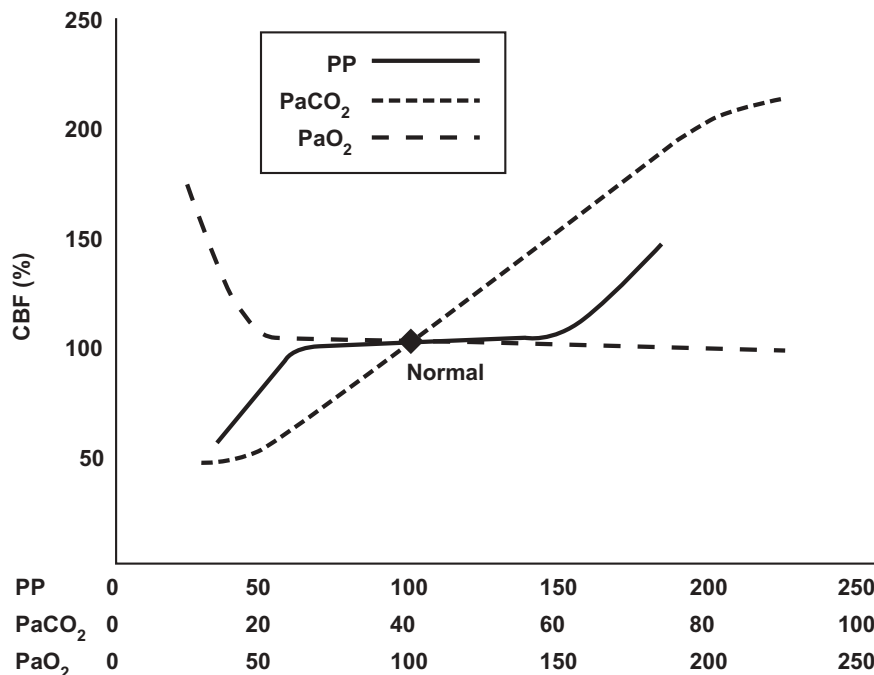
Fig. 5.1   The effects of cerebral perfusion pressure (PP), $PaCO_2$, and PaO_2 on cerebral blood flow. Reproduced with permission from Barash, P.G. (2001) *Handbook of Clinical Anesthesia*, 4th edn. Lippincott Williams & Wilkins, Baltimore, MD.

D. Cerebral blood flow

- o   Normal blood flow in humans is 55 ml/100 g/min.
- o   Flow is greatest in neonates and declines with age.
- o   Blood flow remains constant over a wide range of oxygen and carbon dioxide partial pressures due to *autoregulation* (see Fig. 5.1).
- o   Autoregulation maintains constant brain blood flow over a range of mean systemic blood pressures (60–130 mmHg). Autoregulation is dependent on two processes:
    - –   Vascular smooth muscle responses which occur over 30–40 seconds.
    - –   Neural mediated vasodilation through the VIIth cranial nerve.
    - –   *Atropine* administration may interfere with this mechanism.

E. Cerebral perfusion pressure (PP)

- o   Is the difference between mean systemic blood pressure and intracranial pressure, and should be at least 60 mmHg.
- o   When the perfusion pressure is below this value or cardiac output decreases to less than half normal values, cerebral circulation becomes insufficient.

F. Cerebrospinal fluid (CSF)

- o   Cerebrospinal fluid is contained between the *arachnoid* and *pia mater*.
- o   It acts as a cushion and support for the brain.

o   Changes in brain volume can be offset by CSF production and absorption.

o   The subarachnoid space does not communicate with the subdural space, but is continuous with the ventricles of the brain through medial and lateral connections in the roof of the fourth ventricle. Separations of the arachnoid and pia mater form the cerebromedullary cistern or cisterna magna.

o   Samples of CSF can be obtained from lumbar puncture or through the cisterna magna, although the latter technique carries a higher risk.

o   The composition of CSF is tightly regulated. CSF pH remains about 7.33 even with large changes in plasma pH.

  –   A pH decrease of 0.05 units results in a four-fold increase in ventilation.

o   A potential difference between CSF and blood of about +5 mV is the result of an active transport system.

  – O_2, CO_2, barbiturates, glucose, and lipophilic substances effectively cross the blood–brain barrier.

  –   Inorganic ions, highly dissociated compounds, amino acids, and sucrose cross very slowly.

o   CSF is continuously formed by choroid plexuses in the lateral and third ventricles. The fluid passes into the fourth ventricle, and then into the subarachnoid space around the brain and spinal cord through three foramina.

o   CSF is exchanged every 4 hours and absorption helps maintain pressure at a constant level.

  –   CSF pressure changes with body position, and expiratory efforts such as coughing or straining can sharply increase the pressure.

  –   Most absorption occurs through the subarachnoid villi which protrude into the venous sinuses of the cranium.

II. Central nervous system pathophysiology

A. Seizures

o   Not common in horses, but can occur from brain trauma, bacterial meningitis, viral encephalitis, and possibly, hepatoencephalopathy or vascular accidents.

o   Accidental injection of drugs into the carotid artery can also cause convulsions.

o   In foals, seizures can also be the result of neonatal maladjustment syndrome (brain hypoxia), and idiopathic epilepsy in 3 to 9-month-old Arabians.

o   Anticonvulsants raise the seizure threshold and prevent spread of seizure activity, and decrease the level of activity of abnormal neurons while sparing normal cells.

B. Increased intracranial pressure (ICP)

o   As an intracranial mass expands within the bony cranium, it can cause an increase in ICP. This increase in ICP can be offset by displacement of CSF, blood flow, and displacement of the brain matter. This effect does not continue and once a certain point is reached ICP can rise exponentially.

  –   Sudden increases in ICP can increase the risk of brain herniation.

o   During neuroanesthesia, steps are taken to reduce brain volume as much as possible to offset increases in ICP (see Fig. 5.2).
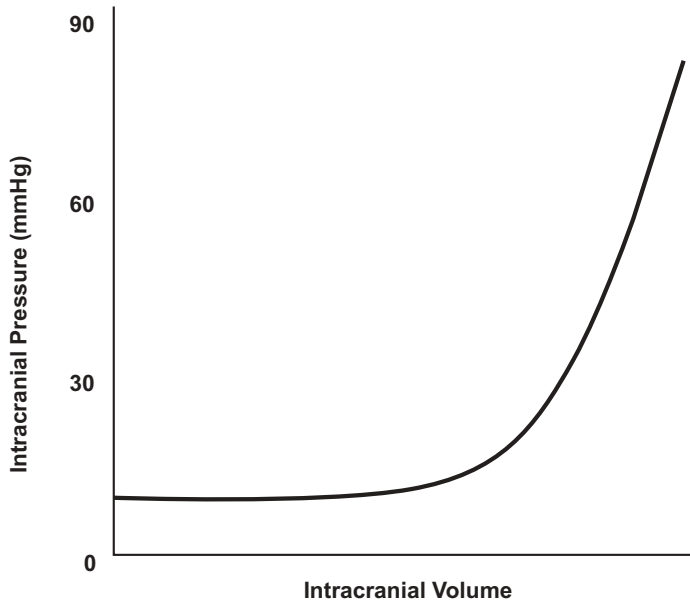
Fig. 5.2 The effects of intracranial volume changes on intracranial pressure. Reproduced with permission from Barash, P.G. (2001) *Handbook of Clinical Anesthesia*, 4th edn. Lippincott Williams & Wilkins, Baltimore, MD.

III. Neuroanesthesia

- o Anesthetic drugs and manipulations performed during anesthesia can affect the following.

A. Cerebral metabolic rate

- o *Normal*: In humans, O_2 consumption is 3.3 ml/100 g/minute similar to that of working skeletal muscle.
  - – In conditions whereby the level of consciousness is depressed, the cerebral metabolic rate is decreased.
- o Oxygen consumption decreases by 20% during hypoglycemia, 40% during general anesthesia, and 3% during sleep.
- o Hypothermia decreases O_2 consumption by 15–20%.

B. Cerebral blood flow and perfusion pressure

- o *Anesthetic drugs* can modify cerebral blood flow and cerebral metabolic rate (see Table 5.1).
  - – These changes can be affected by the presence or absence of intracranial pathology, and also may be influenced by hypoxemic or hypercapnic states.
  - – Cerebral vasodilation often occurs with volatile anesthetics and this may become a problem in disease states when high ICP is already present. The increase in blood volume within the cranium could increase ICP further.

Table 5.1 Effects of drugs on neurophysiology of the brain.

Drug	Cerebral blood flow	Cerebral metabolic O_2 requirements	Direct cerebral vasodilation	Seizure potential
Xylazine	–	?	No Vasoconstrictor	High dose: Anticonvulsant Low dose: Proconvulsant
Acepromazine	–	NC		Possibly proconvulsant
Ketamine	No change with IPPV ++ with hypercapnia	+	Yes, especially with hypercapnia	
Thiopental	–	–	No	Anticonvulsant
Ketamine/diazepam	+	+	?	?
Propofol	–	–	No	Anticonvulsant
Midazolam	–	–	No	Anticonvulsant
Guiaifenesin	?	?	?	Depresses EEG
Halothane	+++	–	Yes	No effect
Isoflurane	+ or NC	–	Yes	No effect
Sevoflurane	+ or NC	–	Yes	No effect

NC = No change, + = increase, – = decrease.

- Drugs which produce a degree of cerebral vasoconstriction may be more useful, especially if they also decrease cerebral metabolic rate.

Increased PaCO$_2$
  o Will increase cerebral blood flow and intracranial volume through vasodilation.
    - This could be detrimental in patients with existing increased ICP.
    - Mechanical ventilation is warranted to ensure PaCO$_2$ values are kept between 30–35 mmHg to reduce the risk of increasing ICP.
    - Excessive ventilation to below this figure will cause more vasoconstriction and lead to poor perfusion of some parts of the brain.

Positive pressure ventilation
  o This is necessary for patients with increased ICP. However, venous return is impeded during the inspiratory phase, and this can cause ICP to rise.
  o High mean airway pressures and over-aggressive ventilation should be avoided.

Venous return
  o In patients with increased ICP, compression of the jugular veins should be avoided to prevent further increases in ICP.

Head position
  o The head should be positioned at the level of the heart, and not below, in order to maintain perfusion pressures and avoid increasing ICP.

C. Autoregulation

- It is important to select drugs that will preserve the brain's ability to autoregulate blood flow.
- Mean arterial blood pressure should be kept in the range within which autoregulation can function (60–130 mmHg), in order to preserve perfusion.
- Patients should be well oxygenated and hypercarbia prevented.

D. Brain protection strategies

- Drugs which decrease cerebral metabolic oxygen demand confer a degree of protection to the brain.
  - The effect of *ketamine* on metabolic rate is debatable. Some studies report decreases while others report increases.
  - The effects of alpha$_2$ adrenergic agonists are not well known.
- *Hypothermia* will decrease metabolic oxygen demand by approximately 20%, and cerebral blood flow decreases 5–7% per °C decrease.

E. Monitoring

Respiratory system
- The $PaCO_2$ should be kept between 30 and 35 mmHg.
- End-tidal capnography often underestimates $PaCO_2$; therefore, arterial blood gas analysis should be used to periodically check the accuracy of the capnogram.
- Avoid high mean airway pressures which might impede venous return and increase ICP.

Cardiovascular system
- Direct arterial pressure monitoring should be performed.
- A cerebral perfusion pressure of at least 60 mmHg should be maintained.
- Arterial pressures should be maintained using fluid therapy, inotropes, and volatile anesthetic reduction techniques.

F. Deliberate hypotension techniques

- In order to reduce blood loss during brain surgery, deliberate hypotension has been employed.
- This technique aims to produce a mean arterial blood pressure of 50 mmHg for short periods of time.
- While this may be feasible in foals, it may cause other problems in adults such as postanesthetic myopathy.

IV. Neuroanesthesia for specific procedures

A. Diagnostic procedures

CSF withdrawal
- CSF is usually obtained using lumbar puncture and horses can be sedated with *xylazine* for this procedure.

- o CSF withdrawal from the cisterna magna will require careful positioning and general anesthesia.
  - – *Xylazine* premedication followed by induction with *thiopental* can be used, although *ketamine* has also been used as an induction agent if the risk of seizures or increased ICP is not present.

Neuroradiology (myelography, MRI, and CT)
- o General anesthesia is often required to facilitate CT or MRI scans.
  - – The special requirements of an MRI unit confine the anesthesia to easily performed injectable techniques unless one uses an MRI compatible inhalational anesthetic machine.
  - – These are commercially available for small animals and therefore inhalational anesthesia can be performed in small foals using these machines.
- o In *adults*, anesthesia is usually maintained using an α_2 agonist, *guaiphenesin*, and *ketamine* in combination. If there is a risk of increased ICP or seizures, *thiopental* can be used instead.
  - – With increased ICP, IPPV should be used to maintain $PaCO_2$ between 30 and 35 mmHg.
- o Inhalational anesthesia can be used in adults if a CT scan is planned.

Contrast media
- o Iodinated contrast agents are often administered during CT and MRI.
  - – Adverse reactions to *diatrizoate* have been reported in anesthetized horses.

B. Increased intracranial pressure

Head trauma, abscess, and tumor removal
- o The likelihood that surgery will be required in a horse with increased ICP is *rare*, but it could be performed for tumor resection or for craniotomy to allow drainage of an intracranial abscess.
  - – Horses may already be mentally depressed due to increased ICP, and drug doses should be reduced accordingly.
  - – Sedatives should not be used in horses with head trauma unless necessary (e.g. displaying agitation or aggression), since neurological evaluation is more difficult in a sedated animal.

Preparation
- o *Mannitol* may be required to reduce ICP and can be given before induction (0.15 – 2.5 g/kg IV over 20 minutes).
- o Fluid balance should be assessed and corrected.
  - – Avoid excessive doses of crystalloids in case of worsening cerebral edema.
  - – Consider using hypertonic saline and/or colloids for head trauma patients, especially foals.

Sedation, premedication and induction
- o Neonatal foals sedate well with *diazepam* (0.02–0.1 mg/kg, IV).
  - – *Butorphanol* may be added (0.05 mg/kg IV).

Induction in foals
- o Can be provided by gentle naso-tracheal intubation or mask-down inhalational techniques using *isoflurane* or *sevoflurane*.
  - – Avoid excessive stimulation of the larynx during intubation to avoid catecholamine release which can increase ICP.
  - – *Ketamine*/benzodiazepine combinations have been shown to increase ICP and not obliterate the catecholamine response to intubation, and are therefore not recommended.

Sedation of adult horses
- o Low doses of *xylazine* may be used.
- o The head should be kept in a raised position so that a low head carriage does not increase ICP.

Maintenance of anesthesia
- o *Isoflurane* or *sevoflurane* are better choices than *halothane*.
- o N_2O is probably not advisable since it increases cerebral blood flow and cerebral metabolic rate when combined with a volatile agent.
- o Since volatile agents increase cerebral blood flow through vasodilation, techniques should be employed to limit this.
  - – A continuous infusion of *lidocaine* or *fentanyl* can also be used to reduce volatile anesthetic MAC.
  - – *Propofol* infusions have been used, with success, in dogs and humans to provide anesthesia, and can be used to reduce the volatile agent MAC. This may be economically feasible with foals.
- o Horses should be ventilated to a $PaCO_2$ between 30 and 35 mmHg.

C. Cerebral edema

- o Global cerebral edema may result from injury or another cause, such as after a successful resuscitation from cardiac arrest.

Drug-induced decompression
- o May be obtained through the use of:
  - – *Mannitol* (0.15–2.5 g/kg, IV over 20 minutes).
  - – Loop diuretics (e.g. *furosemide* 0.75–1.0 mg/kg, IV).
  - – *Dimethylsulphoxide* (*DMSO*) (1.0–2.0g/kg as a 10% or 20% solution).
  - – The use of *dexamethasone* (0.3–0.6 mg/kg, IV) to reduce ICP is controversial.
    - ■ Steroids stabilize blood–brain barrier permeability, but the gluconeogenic effects may worsen brain injury.
  - – Further decrease in ICP may be necessary through the use of sedation and mechanical ventilation ($PaCO_2$ 30–35 mmHg).

Hyperventilation
- o In *neonatal foals*, sedation and tolerance of nasotracheal tube can be obtained using *midazolam* infusions, or low-dose *propofol* infusions.
  - – Neonatal foals may have a reduced ability to metabolize drugs so signs of deepening sedation indicate a need to reduce the amount of drug administered.

- – Care should be directed towards life support during long-term sedation, including the provision of nutrition.
    - o *Adult horses* could be sedated with low-dose *xylazine*, induced with *thiopental*, and maintained with *guaiphenesin*, *thiopental*, or possibly *isoflurane*.
        - – The ability to use IPPV to hyperventilate horses and maintain their $PaCO_2$ will be considerably affected by the presence of ventilation/perfusion mismatch and the time required to maintain the horse in recumbency. This technique is probably not feasible in adult horses.

D. Seizures

- o Sedatives (e.g. *phenobarbital*, *diazepam*) are used to treat seizures.
    - – Intravenous *phenobarbital* can be used for acute seizures, followed by oral therapy.
    - – *Diazepam* (0.01 mg/kg IV) can be administered for acute seizures because it has a rapid effect.
        - ■ Oxygen and ventilatory support may be necessary if high doses of *diazepam* are used in neonates.

Anesthesia of horses prone to seizures
- o *No studies have been published examining these drugs in seizure-prone horses, but the following points are taken from studies performed in other species.*
- o *Xylazine* (0.5–1.0 mg/kg IV) can be used as a premedicant.
    - – *Xylazine* has been shown in other species to have proconvulsant activity at low doses and anticonvulsant activity at sedative doses.
- o *Acepromazine* is not recommended as other phenothiazines have been shown to reduce the seizure threshold.
- o *Ketamine* has also been shown to increase the chance of seizures in patients with a known history of seizure activity.
    - – Since *diazepam* is an anticonvulsant, the combined use of *diazepam* and *ketamine* may be safe to use.
    - – However, *thiopental* is probably a better choice.
- o *Guaiphenesin* has been shown to decrease the EEG in normal subjects and may be used in seizure-prone horses.
    - – A combination of *thiopental* (2 g) in 1 liter 5% *guaiphenesin* administered at an approximate rate of 2.0–2.5 ml/kg/h, IV, may be used to continue anesthesia if necessary.

V. Neuropathy as a result of anesthesia (see Chapter 21)

6   The autonomic nervous system

Christine Egger

The ANS is the portion of the nervous system that controls visceral functions such as arterial blood pressure, heart rate, gastrointestinal motility and secretion, urinary bladder emptying, sweating and body temperature, as well as a number of other important body functions.

I. General organization of the ANS (functional anatomy)

- The autonomic nervous system (ANS) is anatomically divided into the *central* and *peripheral* nervous systems and functionally divided into the *sympathetic* (adrenergic) nervous system (SNS) and the *parasympathetic* (cholinergic) nervous system (PNS).

A. Central autonomic nervous system

- The *hypothalamus* is the principal site of ANS integration (e.g. blood pressure control, thermoregulation, stress response).
- The *medulla oblongata* and *pons* contain the centers for hemodynamic and ventilatory control.

B. Peripheral autonomic nervous system

- *Pre-ganglionic neurons* are myelinated, rapidly conducting, originate in the CNS, and synapse in an autonomic ganglion.
- *Post-ganglionic neurons* are unmyelinated, slower conducting, arise from the autonomic ganglia, and are distributed to effector organs.
- The *SNS* (*paravertebral*) *ganglia* are located nearer to the spinal cord than to the innervated organ, and the *PNS ganglia* are located in or near the innervated organ.

C. Afferent input

- The ANS centers in the brain stem act as relay stations for control of activities initiated at higher levels of the brain, such as the hypothalamus and cerebrum.
- Visceral sensory signals entering the autonomic ganglia, spinal cord, brain stem, or hypothalamus elicit reflex responses which control the activity of visceral organs.

D. Efferent output

- Efferent autonomic signals are transmitted to the body through two major subdivisions of the ANS, the SNS and PNS. (See later discussion.)

II. Physiology of the ANS

A. Neurotransmitters

o *Acetylcholine* (ACh) and *norepinephrine* (NE) are the main neurotransmitters.
o All preganglionic neurons are *cholinergic* in both the SNS and PNS nervous systems.
o Most of the postganglionic neurons of the PNS system are *cholinergic*, while most postganglionic SNS neurons are *adrenergic*.
o The postganglionic SNS nerve fibers to the sweat glands and the piloerector muscles are *adrenergic* (β_2) in horses.

B. Synthesis, duration of action, and degradation of ACh

o ACh is synthesized within the axoplasm in the terminal endings of cholinergic nerves.

$$\text{Acetyl-CoA + Choline} \xrightarrow{\textit{Choline acetyltransferase}} \text{Acetylchoine}$$
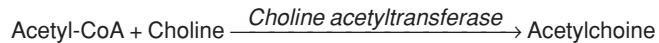
o The ACh is transported to the interior of the vesicles where it is stored in a highly concentrated form until it is released along with ATP.
o After release, ACh persists in the tissue for a few seconds, then most of it is split into an acetate ion and choline by the enzyme *acetylcholinesterase*.

C. Synthesis, duration of action, and removal of NE

o Synthesis of norepinephrine begins in the axoplasm of the terminal nerve endings of adrenergic nerve fibers and is completed inside the vesicles.
o In the *adrenal medulla*, this reaction goes one step further and transforms about 85% of the norepinephrine into epinephrine.
o After secretion, NE is rapidly (within a few seconds) removed from the secretory site.

D. Receptors on the effector organs

o *Cholinergic receptors* are subdivided into *muscarinic* and *nicotinic*.
   – *Muscarinic receptors* are found in all effector cells stimulated by the post-ganglionic PSN neurons, as well as in those stimulated by the postganglionic SNS cholinergic neurons. Subtypes of muscarinic receptors are described in Table 6.1.
   – *Nicotinic receptors* are found in the synapses between the preganglionic and postganglionic neurons of the SNS and PNS and at the neuromuscular junction.
   – ACh is the neurotransmitter at all cholinergic receptors;
o *Adrenergic receptors* are subdivided into *alpha* (α_1 and α_2), *beta* (β_1 and β_2), and *dopaminergic* (DA) (found in the CNS).
   – Norepinephrine (NE) excites α receptors more than β receptors.
   – Epinephrine (EPI) excites both types of receptors approximately equally.

Table 6.1   Muscarinic receptor subtypes.

	M1	M2	M3	M4	M5
Location	● CNS ● Stomach	● Heart ● CNS	● CNS ● Salivary glands; airway smooth muscle	● CNS ● Heart?	● CNS
Clinical effects	H^+ secretion	Bradycardia	Salivation	?	?

III. Function of the adrenal medulla

A. SNS innervation of the adrenals

- Stimulation of the SNS nerves to the adrenal medulla causes large quantities of EPI and NE to be released into the bloodstream.
- About 80% of the secretion is EPI and 20% is NE.

B. Effect of NE release from adrenals

- The circulating NE causes constriction of most of the blood vessels, increased activity of the heart, inhibition of the gastrointestinal tract, and dilation of the pupils.

C. Effect of EPI release from adrenals

- EPI, because it has greater affinity for β receptors, has a more profound effect on cardiac stimulation than does NE. However, NE is a more potent vasoconstrictor.
- NE greatly increases the total peripheral resistance and increases arterial pressure, whereas epinephrine raises the arterial pressure to a lesser extent, but increases the cardiac output considerably more due to its excitatory effect on the heart.

IV. Autonomic effects on the cardiovascular system

A. The heart

- SNS stimulation increases heart rate and contractility.
- PNS stimulation decreases heart rate and can result in asystole.
- Postsynaptic α_2 receptors exert a positive inotropic effect and contribute to development of cardiac dysrhythmias.
- Postsynaptic β_1 receptors and presynaptic β_2 receptors play similar roles in increasing heart rate and myocardial contractility.

B. Systemic blood vessels

- SNS stimulation constricts most systemic blood vessels, especially those of the abdominal viscera and the skin of the limbs.
- PNS stimulation has almost *no effect* on most blood vessels.

o   Presynaptic α_2 vascular receptors mediate vasodilation, whereas postsynaptic α_1 and α_2 vascular receptors mediate vasoconstriction.

o   Postsynaptic α_2 vascular receptors predominate in the venous circulation.

o   Postsynaptic α_2 receptor activation causes arterial and venous vasoconstriction.

o   Postsynaptic β receptors are predominantly β_2 and mediate vasodilation.

C. Effect of SNS and PNS stimulation on arterial pressure

o   SNS stimulation increases cardiac contractility and resistance to flow, which usually causes the arterial pressure to increase greatly.

o   PNS stimulation decreases cardiac contractility but has virtually no effect on peripheral vascular resistance.

o   The usual effect of PNS stimulation is a slight fall in pressure.

D. Cardiovascular autonomic reflexes

o   *Arterial baroreceptors* are stretch receptors located in the carotid sinus and aortic arch.

o   When stretched by high pressure, signals are transmitted to the brain stem, which inhibit the SNS impulses to the heart and blood vessels.

o   There is reduced inhibition of SNS tone if arterial pressure falls (*baroreceptor reflex*).

o   *Venous baroreceptors*, located in the right atrium and great veins, produce an increased heart rate when the right atrium is stretched by increased filling pressure (*Bainbridge reflex*).

V. Autonomic effects on the pulmonary system

•   Muscarinic receptors mediate bronchoconstriction and increased mucus secretion.

• β_2 receptors mediate bronchial smooth muscle *relaxation* and increased mucus secretion. (See Table 6.2.)

Table 6.2   Comparative pharmacology of selective β_2 adrenergic bronchodilators.

Agent	β_2 selectivity	Peak effect (minutes)	Duration of action (hours)
Albuterol	+++++	30–60	4
Metaproterenol	+++	30–60	3–4
Terbutaline	++++	60	4
Salmeterol	++++		> 12

VI. Pharmacology of the ANS

A. Drugs that act on adrenergic effector organs (sympathomimetic drugs)

o   Adrenergic agonists include vasopressors (e.g. *phenylephrine*) and inotropes (e.g. *dobutamine*).

Table 6.3   Principal sites of action of adrenergic agonists.

Agent	α_1	α_2	β_1	β_2	DA_1	DA_2	Mechanism
Methoxamine	+++++	?	0	0	0	0	Direct
Phenylephrine	+++++	?	+/–	0	0	0	Direct
Norepinephrine	+++++	+++++	+++	0	0	0	Direct
Epinephrine	+++++	+++	+++++	++	0	0	Direct
Ephedrine	++	?	+++	++	0	0	Indirect + direct
Dopamine	+ to +++++	?	+++	++	0	0	Direct
Dobutamine	+/–	?	++++	++	0	0	Direct
Dopexamine	0	0	+	++++	+	?	Direct
Isoproterenol	0	0	+++++	+++++	0	0	Direct

+ = Increase, – = decrease, 0 = no change.

Table 6.4   Cardiovascular effects of adrenergic agonists.

Agent	HR	CO	SVR	VR	MAP	Dysrhythmias	RBF	AR	CNS stimulation
Methoxamine	–	–	+++	0	+++	0	–––	0	0
Phenylephrine	–	–	+++	++	+++	0	––	0	0
Norepinephrine	–	–	+++	++	+++	+	–––	0	0
Epinephrine	++	++	+	+	+	+++	–––	–––	+
Ephedrine	++	++	++	++	++	++	+/–	–––	+
Dopamine	+	++	+	+++	+	+	+++	0	0
Dobutamine	+	+++	0	+/–	+	+/–	++	0	0
Isoproterenol	+++	+++	–––	–––	+/–	+++	–	–––	+

HR = Heart rate, CO = cardiac output, SVR = systemic vascular resistance, VR = venous return, MAP = mean arterial pressure, RBF = renal blood flow, AR = airway resistance. +, Increase; –, decrease; 0 = no change.

- ○ Most adrenergic agonists activate α and β receptors, with the predominant pharmacologic effect being the expression of this mixed receptor activation. (See Table 6.3.)
- ○ Hemodynamic effects evoked by adrenergic agonists include changes in heart rate (*chronotropism*), cardiac contractility (*inotropism*), conduction velocity of the cardiac impulse (*dromotropism*), cardiac rhythm, and systemic vascular resistance (SVR). (See Table 6.4.)
- ○ Effects of these drugs on capacitance veins (venous return) may be as important as inotropic actions and more important than arteriolar effects.

B. Drugs that cause release of NE from nerve endings

- o Certain drugs have an indirect sympathomimetic action, rather than directly exciting adrenergic effector organs, and cause release of NE from its storage vesicles in the SNS nerve endings (e.g. *ephedrine*).

C. Drugs that have a PNS potentiating effect (anticholinesterase drugs)

- o *Neostigmine*, *pyridostigmine*, and *edrophonium* are used for reversal of non-depolarizing neuromuscular blockade.
- o These drugs inhibit *acetylcholinesterase*, preventing rapid destruction of ACh so that it accumulates at muscarinic and nicotinic receptors.
- o Simultaneous administration of an anticholinergic prevents unwanted muscarinic signs (bradycardia, salivation, bronchospasm, intestinal hypermotility) without preventing the nicotinic affects of ACh.

D. Drugs that block cholinergic activity at effector organs (antimuscarinic drugs) (see Table 6.5.)

- o Block the action of ACh on the muscarinic type of cholinergic effector organs, but do not affect the nicotinic action of ACh on the postganglionic neurons or on skeletal muscle (e.g. *atropine*).

Table 6.5   Comparative effects of anticholinergic drugs.

Anticholinergic	Sedation	Salivary and respiratory secretions	↑HR	Relax smooth muscle	Mydriasis	↓Gastric H^+ secretion	GIT tone	Alter fetal HR
Atropine	+	−	+++	++	+	+	−−−	+
Glycopyrrolate	0	−−	++	++	0	+	−−−	0
Scopolamine	+++	−−−	+	+	+++	+	−	+

+ = Increase, − = decrease, 0 = no change.

7 Fluids, electrolytes, and acid–base

Fluid therapy

Craig Mosley

- Anesthetics reduce myocardial contractility, cardiac output, and vascular responsiveness (baroreceptor response), and cause vasodilation.
- These alterations can lead to a reduction in arterial blood pressure, increased intravascular (due to vasodilation) volume and a reduction in tissue perfusion, predisposing to complications (e.g. myopathy).
- *Intravenous fluid therapy* is used during anesthesia to:
  - Counteract the hemodynamic effects of general anesthetics.
  - Establish IV access for emergency drugs and intraoperative support.
  - Replace the insensible fluid losses and the fluid loss associated with surgery.
- Designing a perioperative fluid plan requires careful evaluation of physical examination findings, history (sweating, blood loss, and duration of problem), laboratory tests and the pathophysiology of concurrent disease.
- Horses with hypovolemia and/or dehydration should have appropriate fluid support *prior* to the induction of anesthesia.

I. Composition of body fluids

A. Adults

- Volume (liters) of total body water (TBW) is 60–65% of an adult horse's weight (kg).
- TBW can be divided into *intracellular fluid volume* (ICFV) which is ~ 40% of body weight, and the *extracellular fluid volume* (ECFV) which is 20–25% of body weight.
- Extracellular fluid can be subdivided into *plasma volume* (PV) which is 4–6% of body weight, and interstitial fluid volume (IFV) which is ~ 15% of body weight.
  - The ECFV also includes lymph and small amounts of transcellular fluids (e.g. sweat, gastrointestinal secretions, and cerebrospinal, synovial, peritoneal, and pleural fluids).
- *Blood volume* (liters) is ~ 8% of body weight (kg) and is composed of the plasma volume and the intracellular volume of red blood cells.

B. Neonates

- At birth, TBW may be 75–85% of body weight.
- *Blood volume* (liters) in neonatal foals is approximately 9% of body weight (kg).
  - Much of this additional fluid is contained in the interstitial space, allowing neonates to translocate fluid from the interstitial to the intravascular space in response to dehydration or hemorrhage.

- ○ Precapillary tone is poorly developed and capillary permeability may be increased.
- ○ Neonates are less able to maintain an isotonic fluid load in the intravascular space and may be more susceptible to the development of interstitial *edema*.
  - – Colloids may also pass through the leaky capillaries into the interstitium, exacerbating fluid retention.
- ○ Foals may be less able to compensate for increased fluid loads and may have a tendency to retain fluids, leading to edema.

II. Distribution of body fluids

- ● *Aldosterone* (enhances sodium reabsorption), *arginine vasopressin* (enhances water reabsorption), and *atrial natriuretic peptide* (enhances sodium and water excretion) all regulate extracellular fluid volume.

A. Fluid dynamics between the intra- and extracellular spaces

- ○ Fluid spaces are contiguous, and almost all cell membranes are permeable to water.
- ○ The volume of the extracellular and intracellular fluid space is determined by the number of osmotically active particles in each space.
- ○ Osmolarity refers to the number of osmoles (particles) per liter of solution.
  - – *Effective osmoles* are particles that cannot cross cellular membranes.
- ○ Sodium is the principal extracellular and potassium the principal intracellular osmole.
  - – Cell membranes are permeable to Na and K, but these ions act as effective osmoles because they are restricted to their respective compartments by the Na–K ATPase pump located in the cell membrane.
- ○ Intracellular and extracellular fluid volumes are determined by the amount of TBW and the ratio of intracellular potassium and extracellular sodium.

B. Fluid dynamics between intravascular and interstitial space

- ○ Colloid oncotic pressure maintains fluid balance between the intravascular and interstitial space and is described by *Starling's equation*.
  - – Changes in any variable alter the net influx or efflux of water from the intravascular space.

$$\text{Net fluid flux } (J_v) = K_{fc}[(P_c - P_i) - \sigma(\pi_p - \pi_i)]$$

where K_{fc} = Filtration coefficient
P_c = Capillary hydrostatic pressure
P_i = Interstitial hydrostatic pressure
σ = Reflection coefficient
π_p = Capillary oncotic pressure
π_i = Interstitial oncotic pressure

- ○ *Albumin* is responsible for the majority of intravascular oncotic pressure (60–70%) with *globulins* being responsible for the remainder.
  - – Albumin exerts a slight negative charge that helps retain cations within the intravascular space (*Gibbs–Donnan effect*).
- ○ Electrolyte compositions of intravascular and extravascular fluid are very similar.

III. Distribution of infused fluids

- The tonicity and electrolyte composition of intravenous fluids will determine their distribution among the body compartments.
  - *Tonicity* refers to the effective osmolarity in relation to ECF or plasma.
- Sodium is the major *effective* osmole in most fluids.
  - Although K is also an effective osmole, its cardiotoxic effects limit the amount that can be administered.
- The osmolarity of extracellular fluid is 285 ± 10 mOsm/liter while the osmolarity of plasma is slightly higher due to the contributions of plasma proteins.
- *Hypotonic* solutions distribute to the extracellular and intracellular spaces.
  - Some hypotonic fluids (e.g. 5% dextrose) are prepared as isotonic solutions, but the osmoles (dextrose) are rapidly metabolized *in vivo* leaving *free water*, which is a hypotonic solution.
- *Isotonic* fluids have a [Na] similar to extracellular fluid and distribute primarily to the extracellular space.
- *Hypertonic* fluids with [Na] in excess of extracellular space concentrations draw fluid from the intracellular space expanding the intravascular volume above the volume of fluid administered.

IV. Types of fluids

A. Crystalloids

- Are solutions containing electrolytes and other small solutes (e.g. glucose).
- Crystalloids may be classified as either *replacement* or *maintenance*.
  - *Replacement solutions* have electrolyte composition similar to extracellular fluid or plasma. Replacement fluids are *isotonic*.
  - *Maintenance solutions* have electrolyte compositions appropriate to replace daily sensible and insensible losses. Solutions are often *hypotonic*.

Hypotonic crystalloids
- Rarely used.
- Distribute to the ECFV as well as the ICFV.
- Limited role for intravascular volume expansion.
- May precipitate the formation of edema if large quantities are used.
- *Examples include*: Plasma-Lyte 56, 0.45% NaCl & 2.5% dextrose, 5% dextrose.

Isotonic crystalloids
- Most common fluid for maintenance therapy during anesthesia.
- Mainly used for replacing deficits in hypovolemia and/or dehydration.
- Recommended administration rates:
  - Daily maintenance rate ≈65 ml/kg/day.
  - Shock rate for rapid resuscitation ≈45 ml/kg/h.
  - Anesthesia maintenance rate ≈5–10 ml/kg/h.
    - These rates are guidelines and should be adjusted to reflect individual requirements.

- ■ Blood pressure, heart rate, capillary refill time and serial PCV, TP, and lactate assessment can be used to guide therapy.
- ○ Approximately 75% will be redistributed to the interstitial space.
  - – Less than 20% remains in the intravascular space after 2 h.
  - – ~ 10% remains after 3 h.
- ○ Crystalloid solutions can be *alkalinizing* or *acidifying* depending on added base precursor (e.g. lactate or acetate) and the *strong ion difference*.
  - – *Lactate* is a mild alkalinizing agent when metabolized in the liver.
  - – *Acetate* does not require liver metabolism to exert its alkalinizing effects.
    - ■ In hypovolemia, rapid bolus may cause transient vasodilation and hypotension.
- ○ Calcium-containing solutions should *not* be administered in the same line as blood or plasma.
  - – Calcium may *bind citrate* and cause *coagulation*.
- ○ Sodium bicarbonate may precipitate in calcium-containing solutions.

Hypertonic crystalloids
- ○ Commonly used for emergency resuscitation of hypovolemic patients.
- ○ 7.2% NaCl is the most commonly used.
  - – Osmolarity ~ 2400 mOsm/liter.
- ○ Recommended dose is 2–4 ml/kg administered over 15 minutes.
- ○ Following administration, fluid will be drawn from the extravascular to the vascular space increasing plasma volume (~ 5× infused volume).
- ○ Effect on vascular expansion is transient (30–60 minutes) due to redistribution of the NaCl in the extracellular space and to urinary losses.
  - – Appropriate isotonic crystalloid, based on deficits, should be administered following hypertonic saline to maintain intravascular volume.

B. Colloids

- ○ Are aqueous solutions containing macromolecules that do not normally pass through the capillary membrane.
- ○ Used to maintain vascular volume and are useful when large volumes of crystalloid are needed and for oncotic therapy (e.g. hypoproteinemia).
- ○ Can be classified into *synthetic* (complex carbohydrate preparations) and *natural* (albumin-containing blood products).

Synthetic colloids
- ○ Include *dextrans*, *hetastarch* and *pentastarch*.
- ○ Eliminated by glomerular filtration, extravasation, storage in tissues, and via the gastrointestinal tract.
- ○ Can impair coagulation via a direct effect on platelets and clotting factors and indirectly by inducing a mild dilutional coagulopathy.
  - – *Dextrans* tends to have the greatest effect on coagulation.
- ○ Use with caution in patients with anuric or oliguric renal failure, congestive heart failure, pulmonary edema, and intracranial hemorrhage.
- ○ Intraoperative maintenance rates range from 2 to 4 ml/kg/h.
  - – *The recommended daily dose is 20 ml/kg*.

     o Interfere with total solid readings from a refractometer.
        – Refractometer readings will tend to underestimate the increases in colloid oncotic pressure caused by synthetic colloids.

Natural colloids
     o Whole blood and plasma (fresh or frozen) are the most common.
        – *Whole blood transfusions* are indicated for hemorrhagic shock, coagulation disorders, hemolytic crises, and nonresponsive anemias.
        – *Plasma transfusions* are indicated for restoration of plasma oncotic pressure (hypoalbuminemia), coagulation disorders (fresh or fresh frozen only), and treatment of failure of passive transfer in foals.
     o All blood products should be administered through an appropriate administration set that includes a filter.

Other colloid solutions
     o Polymerized ultrapurified bovine hemoglobin has been used in horses and foals to support oxygen carrying capacity, and it has potentially beneficial plasma volume expanding effects owing to its high colloid oncotic pressure.
        – A total dose of 15 ml/kg was used in anemic ponies at a rate of 10 ml/kg/h. One of six ponies developed an *anaphylactoid* reaction during the infusion that resolved once the infusion was discontinued.

Electrolytes

Craig Mosley

I. Sodium

- Physiological roles of sodium include:
     o Maintaining extracellular osmolarity.
     o Maintaining extracellular fluid volume.
     o Development of action potentials.
        – Serum [Na] reflects the ratio of total body sodium to total body water (TBW).
        – Hydration status must be considered for interpretation of [Na].
            ■ A change in [Na] may reflect changes in sodium or changes in TBW.

A. Hyponatremia (<125 mEq/liter)

     o Clinical signs are usually only present in severe hyponatremia.
     o CNS signs include:
        – Lethargy.
        – Central blindness.
        – Seizures and tremors.

- ○ Causes include:
  - – Relative water excess due to:
    - ■ Loss of high sodium containing fluids (e.g. diarrhea, sweating, blood loss).
    - ■ Adrenal insufficiency.
    - ■ Sequestration of fluid.
    - ■ Third-space loss (e.g. ruptured bladder).
  - – False hyponatremia due to:
    - ■ Hyperlipidemia.
    - ■ Hyperproteinemia.
    - ■ Hyperglycemia.
  - – Excessive administration of hypotonic fluids (e.g. 5% dextrose).
- ○ Treatment:
  - – The need for treatment with sodium-rich fluids depends upon severity of clinical signs and chronicity of hyponatremia.
  - – Na^+ deficit = (Desired [Na] − Actual [Na]) × 0.6 × body weight (kg).
  - – Rate of replacement depends upon severity of deficit and the rate of development of hyponatremia.

B. Hypernatremia (>155 mEq/liter)

- ○ CNS signs include:
  - – Lethargy.
  - – Weakness.
  - – Seizures and coma.
- ○ Causes include:
  - – Pure water loss due to:
    - ■ Water deprivation.
    - ■ Respiratory losses (hyperventilation, panting).
  - – Sodium excess due to:
    - ■ Salt intoxication.
    - ■ Feeding electrolytes with no free water.
    - ■ Hypertonic fluid administration (rarely clinically significant).
- ○ Treatment:
  - – Address underlying cause (provide access to water).
  - – If long-standing, correct slowly using hypotonic fluids (e.g. 0.45% NaCl).

II. Potassium

- • Physiological roles of potassium include:
  - ○ Maintaining intracellular osmolarity.
  - ○ Maintaining transmembrane potential.
  - ○ Developing action potentials in muscle and nerves.
- • Serum K is altered by external (intake and output) and internal (distribution of K between intracellular and extracellular fluid) factors.

A. Hypokalemia

- o Signs include:
  - – Cardiac arrhythmias.
  - – Muscle weakness.
  - – Ileus.
- o Causes include:
  - – Altered external balance due to:
    - ■ Diarrhea.
    - ■ Excessive sweat loss.
    - ■ Third space loss.
    - ■ Dietary deficiency/anorexia.
  - – Altered internal balance due to:
    - ■ Metabolic alkalosis.
- o Treatment:
  - – Oral or IV K (*do **not** exceed 0.5 mEq/kg/h*; IV).

B. Hyperkalemia

- o Signs include:
  - – Cardiac arrhythmias (severe when $K^+ > 7.0$ mEq/liter).
    - ■ Broadening and flattening of P wave.
    - ■ Bradycardia.
    - ■ Heart block.
    - ■ Asystole.
    - ■ Fibrillation.
  - – Muscle weakness and fasciculation.
- o Causes include:
  - – False hyperkalemia due to:
    - ■ Hemolysis, resulting from prolonged storage of blood sample without separation.
  - – Altered *external* balance due to:
    - ■ Renal shutdown.
    - ■ Ruptured urinary bladder.
  - – Altered *internal* balance due to:
    - ■ Metabolic acidosis.
    - ■ Vigorous exercise.
    - ■ Hyperkalemic periodic paralysis.
- o Treatment:
  - – It is recommended to reduce $[K^+]$ to < 6 mEq/liter *prior* to induction of anesthesia, because anesthetics exacerbate cardiac arrhythmias.
    - ■ Correct the underlying cause (e.g. dehydration, metabolic acidosis)**.**
  - – Fluids: *Rate and volume dictated by patient status and ongoing alterations.*
    - ■ 0.9% NaCl.
    - ■ Hypertonic fluid if [Na] is low.
  - – *Dextrose* (0.25−0.5 mg/kg, IV) alone or with *regular insulin* (0.05−0.1 U/kg, IV).
    - ■ Dextrose 50% as a slow bolus or diluted to 10% in saline.
    - ■ Dextrose alone may be sufficient to move extracellular K into cells.
    - ■ Regular insulin should not be used without dextrose.

- Calcium gluconate 23% (0.2–0.4 ml/kg, IV).
    - Administer slowly (over 15 minutes).
- $NaHCO_3$ (1–2 mEq/kg, IV) if metabolic acidosis is significant.
    - Administer slowly (over 15 minutes).

III. Chloride

- Chloride should always be interpreted relative to sodium.
- Frequently, alterations in [Cl] are secondary to primary changes in total plasma water.
- $\text{Corrected [Cl]} = \text{Measured [Cl]} \times \dfrac{\text{Normal [Na]}}{\text{Measured [Na]}}$

A. Hypochloremia

- Signs:
    - Similar to hyponatremia and often accompanied by decreases in sodium.
    - Horses may exhibit respiratory evidence of acid–base abnormality.
- Common causes:
    - Relative water excess with a proportional decrease in Na (normal corrected Cl) due to loss of sodium- and chloride-containing fluids.
        - Diarrhea, sweating, blood loss.
        - Sequestration of fluid.
        - Third-space loss (e.g. peritonitis, ruptured bladder).
    - False hypochloremia due to:
        - Hyperlipidemia.
        - Hyperproteinemia.
        - Hyperglycemia.
    - Chloride loss without proportional decrease in Na ($\downarrow$ corrected Cl) due to:
        - Frequently associated with metabolic alkalosis.
        - Chloride sequestration (e.g. stomach or high intestinal obstruction).
        - Furosemide therapy.
- Treatment:
    - Correct the underlying abnormality.

B. Hyperchloremia

- Signs:
    - Variable.
    - Similar to hypernatremia often accompanied by $\uparrow$ in [Na].
    - May exhibit respiratory evidence of acid–base abnormality.
- Common causes:
    - Relative water deficits with a proportional $\uparrow$ in Na (normal corrected Cl) due to:
        - Water deprivation.
        - Respiratory (hyperventilation, panting).
    - Chloride excess without a proportional $\uparrow$ in Na ($\uparrow$ corrected Cl).

- o Frequently associated with a metabolic acidosis from renal tubular acidosis (rare) or *acetazolamide* therapy for HYPP.
- o Treatment:
  - – Correct the underlying abnormality.

IV. Calcium

- Physiologic roles of calcium include:
  - o Excitation–contraction.
  - o Neurotransmission.
  - o Enzyme function.
  - o Cardiac action potential.
  - o Cardiac pacemaker activity.
  - o Bone formation.

A. Hypocalcemia

- o Signs include:
  - – Fatigue.
  - – Tetany.
  - – Synchronous diaphragmatic flutter.
- o Common causes:
  - – Hypoalbuminemia.
  - – Lactation tetany.
  - – Sepsis (decreases ionized calcium).
- o Treatment:
  - – Calcium gluconate (23% 0.5–1.0 ml/kg/h, IV) or elemental calcium (0.1–0.4 mg/kg/min, IV).

B. Hypercalcemia

- o Signs may be non-specific.
  - – May cause cardiac arrhythmias.
- o Common causes:
  - – Chronic renal failure.
  - – Hypervitaminosis D (e.g. dietary supplementation).
  - – Malignancy.
- o Treatment:
  - – In the perioperative period includes 0.9% NaCl infusion and *furosemide* therapy to enhance calcium excretion.

Acid–base physiology

- Acid–base interpretation can be performed using two different methods:
  - o The first is the *traditional* approach, which is based on evaluating plasma [HCO_3^-] and/or base excess to measure disturbances in metabolic acid–base balance.

- ○ The second is the *physicochemical* approach, as described by Peter Stewart (*Stewart method*) and based on the quantification of independent variables (PCO_2, weak acids, and the strong ion difference) and dependent variables (HCO_3^- and H^+ ions).
- *Acidemia* refers to a blood [H^+] above the normal range and a pH below normal.
  - ○ *Acidosis* is a physiological condition that would cause acidemia if it were allowed to go uncompensated.
- *Alkalemia* refers to a blood [H^+] below the normal range and a pH above normal.
  - ○ *Alkalosis* is a physiological condition that would cause alkalemia if it were allowed to go uncompensated.

I. Traditional approach

A. Henderson–Hasselbalch equation

$$pH = pK_a + \log \frac{[\text{base}]}{[\text{acid}]}$$

- – $pH = -\log_{10}[H^+]$.
- – pK_a is the negative logarithm of the constant of dissociation for plasma carbonic acid.
- – The base is represented by HCO_3^- and is regulated by kidney function.
- – The acid is represented by the solubility (expressed as a solubility coefficient *s*) of CO_2 and its partial pressure in arterial blood and is therefore regulated by respiratory function.
- – So $pH = pK_a + \log \dfrac{[HCO_3^-]}{[s \times PaCO_2]}$
- ○ The Henderson–Hasselbalch equation is derived from the reversible hydration reaction for CO_2 and from the reversible ionization of carbonic acid.

$$CO_2 + H_2O \underset{\longleftarrow}{\overset{CA}{\longrightarrow}} H_2CO_3 \underset{\longleftarrow}{\longrightarrow} H^+ + HCO_3^-$$
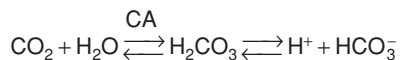
- – Gaseous CO_2 dissolves and combines with water to form carbonic acid.
- – Carbonic anhydrase (CA) in red cells and renal tubular cells allows for this reaction to be up to 1000 times faster than in blood.
- – Carbonic acid is ionized and yields equivalent numbers of H^+ and HCO_3^-.
- – Therefore, HCO_3^- concentrations are dependent on the partial pressure of CO_2 in plasma.

Values for the Henderson–Hasselbalch equation
- ○ $pK_a = 6.1$ (for bicarbonate system).
- ○ $HCO_3^- = 24$ mEq/liter.
- ○ $PaCO_2 = 40$ mmHg
- ○ $s = 0.03$ mEq/liter/mmHg at 37°C.

- o   Therefore, $pH = 6.1 + \log[24 / (0.03 \times 40)]$
  $$pH = 6.1 + \log(24/1.2)$$
  $$pH = 6.1 + \log 20$$
  $$pH = 6.1 + 1.3$$
  $$pH = 7.4$$

B. pH and hydrogen ions

- o   Hydrogen ion concentrations in the body are extremely low (10^{-7} to 10^{-9} equivalent/liter).
- o $[H^+]$ is tightly regulated for enzyme activities and biochemical reactions.
  - – $[H^+]$ is regulated by the lungs (CO_2) and the kidneys (by altering ion secretion).
- o   The higher the $[H^+]$, the lower the pH.
  - –   For pH values in the clinical range (7.2–7.5) the relationship between pH and $[H^+]$ is fairly linear.
    - ■   A pH of 7.5 = $[H^+]$ of 32 nEq/liter
    - ■   A pH of 7.4 = $[H^+]$ of 40 nEq/liter.
    - ■   A pH of 7.3 = $[H^+]$ of 41 nEq/liter.
    - ■   A pH of 7.2 = $[H^+]$ of 62 nEq/liter
- o   Hydrogen ions can be formed from water and can be destroyed by the formation of water.
  - –   It is generally agreed that watery solutions are *neutral* if the concentrations of the hydrogen ions equal the concentrations of the hydroxyl ions ($[H^+] = [OH^-]$), *acidic* if $[H^+] > [OH^-]$, and *alkaline* if $[H^+] < [OH^-]$.
  - –   The $[H^+]$ is always a dependent variable and is in a nonlinear association with PCO_2, with the concentration of fully dissociated electrolytes (often termed 'strong electrolytes') and weak acids (proteins).

C. Buffering

- o   Defined as the ability of a solution to resist change in acidity following the addition of an acid or a base.

The carbonic acid–bicarbonate buffer system
- o   Is the main buffer mechanism of equilibration with the extracellular $[H^+]$.
- o   Carbonic acid is a volatile acid that is controlled by the respiratory system through CO_2 elimination (see Henderson–Hasselbalch equation).

Non-bicarbonate buffer systems
- o   Include proteins (especially hemoglobin but also albumin), phosphate, and ammonium.
  - –   *Hemoglobin* is a more efficient buffer than albumin because of its higher concentration in blood and because of its higher buffer value (0.18 vs. 0.12 mEq/gram/pH).
- o   Inorganic and organic phosphate compounds can function as buffers.
  - –   Inorganic phosphates are major urinary buffers. $H_2PO_4^- \rightleftharpoons HPO_4^{2-} + H^+$.
  - –   Organic phosphates act as intracellular buffers.
  - –   Organic phosphates include 2,3-diphosphoglycerate (2,3-DPG), glucose-1-phosphate, adenosine monophosphate (AMP), adenosine diphosphate (ADP), and adenosine triphosphate (ATP).

- o Ammonium (NH_4^+) is the weak acid of the strong base ammonia (NH_3) and plays an important role in the kidney as a vehicle for removing hydrogen ions from the body.

  $$NH_4^+ \rightleftharpoons NH_3 + H^+$$

  - – Ammonia, generated by enzymatic actions within the renal tubular epithelial cells, is more diffusible into the tubular lumen than ammonium.
  - – The high affinity of ammonia for hydrogen ions produces ammonium ions, which because of their nondiffusible properties are trapped in the lumen and eliminated with the final urine.

D. Base excess

- o Defined as the amount (mmol or mEq) of strong acid or strong base required to titrate extracellular fluid (1 liter) to pH 7.40 with $PaCO_2 = 40$ mmHg at normal body temperature.
- o Base excess quantifies the patient's total base excess or deficit from the normal buffer base at any given pH.
- o It is calculated from the measurement of pH, $PaCO_2$, and hematocrit (as red cells contain most of the buffer content, i.e. hemoglobin).
- o The value for base excess is obtained by multiplying the deviation in standard bicarbonate from normal by an empirical factor (1.2) that is related to the buffering capacity of red cells.
- o It is a true non-respiratory reflection of acid–base status.

E. Primary disturbances in acid–base (see Table 7.1)

- o Four primary disturbances are recognized:
  - – Respiratory acidosis (increased $PaCO_2$).
  - – Respiratory alkalosis (decreased $PaCO_2$).
  - – Metabolic acidosis (decreased base excess or actual $[HCO_3^-]$).
  - – Metabolic alkalosis (increased base excess or actual $[HCO_3^-]$).
- o Combinations of these disturbances can occur as a result of compensatory or acid–base derangements.
- o The body attempts to maintain the HCO_3^- to CO_2 ratio at 20:1 with changes in ventilation or renal function.
  - – In *metabolic acidosis*, hyperventilation is instituted to reduce $PaCO_2$.
  - – In *respiratory acidosis*, renal conservation of HCO_3^- occurs.

Respiratory acidosis (pH < 7.35, $PaCO_2$ > 45)
- o Is the result of an increase in $PaCO_2$ due to ventilatory failure.
  - – Ventilatory failure results from pulmonary disorders, hypoventilation due to CNS depression (anesthetic drugs), and impaired function of respiratory muscles and nerves.
- o Increased $PaCO_2$ causes an increase in blood $[H^+]$ and a decrease in pH.
  - – An acute increase in $PaCO_2$ of 20 mmHg decreases the pH by ~ 0.1.
  - – An acute increase in $PaCO_2$ of 20 mmHg increases the HCO_3^- by ~ 2 mEq/liter.
- o Compensation occurs by renal retention of HCO_3^-, but the process is slow and so acute respiratory acidosis is uncompensated.

Table 7.1 Summary of acid–base disorders.

Disorder	pH	PCO_2	HCO_3^-	Base excess	SID
Respiratory acidosis					
Acute (uncompensated)	↓	↑	N	N	↑
Partly compensated	↓	↑	↑	↑	↑
Chronic (compensated)	N	↑	↑	↑	↑
Respiratory alkalosis					
Acute (uncompensated)	↑	↓	N	N	↓
Partly compensated	↑	↓	↓	↓	↓
Chronic (compensated)	N	↓	↓	↓	↓
Metabolic acidosis					
Acute (uncompensated)	↓	N	↓	↓	↓
Partly compensated	↓	↓	↓	↓	↓
Chronic (compensated)	N	↓	↓	↓	↓
Metabolic alkalosis					
Acute (uncompensated)	↑	N	↑	↑	↑
Partly compensated	↑	↑	↑	↑	↑
Chronic (compensated)	N	↑	↑	↑	↑

- – A simple acute respiratory acidosis usually has a $[HCO_3^-]$ between 24 and 30 mEq/liter.
- – A respiratory acidosis with a $[HCO_3^-] > 30$–32 mEq/liter signifies a chronic respiratory acidosis (e.g. a horse with recurrent airway obstruction) or a concurrent metabolic alkalosis.
- o Treatment of acute respiratory acidosis during anesthesia is usually corrected by instituting mechanical ventilation.
  - – If it does not correct, other causes of hypoventilation, such as airway obstruction, should be investigated and eliminated.

Respiratory alkalosis (pH>7.45, $PaCO_2$<35 mmHg)
- o Generally results from a decrease in $PaCO_2$ (<35 mmHg) due to increased alveolar ventilation.
  - – Mechanical hyperventilation during anesthesia is a potential cause.
  - – Other causes include hypoxia, CNS infection, trauma, pain, and pulmonary edema.
- o The decreased $PaCO_2$ causes a decrease in blood $[H^+]$ and an increase in pH.
  - – An acute decrease in $PaCO_2$ by 10 mmHg causes the pH to increase by ~ 0.1.
  - – An acute decrease in $PaCO_2$ by 10 mmHg causes HCO_3^- to decrease by 2 mEq/liter.
- o *Treatment* should address the underlying cause; during anesthesia this generally involves decreasing alveolar ventilation.

Metabolic acidosis (pH<7.35, HCO_3^-<20 mEq/liter)
- o Is the result of a reduction in plasma $[HCO_3^-]$.
- o Bicarbonate loss may occur *directly* through the gastrointestinal tract or through the kidney.

- o Bicarbonate loss may occur *indirectly* from an increase in the H^+ load from either endogenous or exogenous sources, and from a decrease in the kidney's ability to excrete acid.
  - – A decrease in $[HCO_3^-]$ of 10 mEq/liter decreases pH by 0.15.
- o Diarrhea (leading to cardiovascular collapse and hypoxin) and lactic acidosis are common causes.
- o Compensation occurs *initially* by alveolar hyperventilation, but renal compensation (HCO_3^- retention) must also occur to correct metabolic acidosis, and this process may take a few days.
- o *Treatment* is generally recommended if the pH is < 7.2.
  - – Complete correction is not recommended as this may lead to a metabolic alkalosis and hypernatremia and an increased risk of cardiac dysrhythmias.
  - – A pH of 7.25 is a reasonable objective.
  - – *Sodium bicarbonate dose* is commonly calculated as follows:

    $$NaHCO_3 \text{ (mEq)} = \text{Body mass (kg)} \times HCO_3^- \text{ deficit} \times 0.3$$
    - ■ HCO_3^- deficit = normal HCO_3^- − actual HCO_3^-
    - ■ 0.3 represents the volume of distribution of HCO_3^- in extracellular fluid. Higher values (0.4–0.5) are quoted for neonates due to their increased ECF volume.
  - – *Example*: A 500 kg horse with a plasma HCO_3^- of 10 mEq/liter and pH 7.18:

    $$NaHCO_3 \text{ (mEq)} = 500 \times (24 - 10) \times 0.3$$
    $$= 500 \times 14 \times 0.3$$
    $$= 2100 \text{ mEq}$$
  - – It is generally recommended to administer one-third to one-half of the calculated dose over a few hours, in association with volume expansion (e.g. balanced electrolyte solutions).
  - – Bicarbonate therapy is only recommended if the cause of the HCO_3^- deficit is related to true HCO_3^- losses (e.g. diarrhea or renal tubular acidosis). Otherwise, fluid support is usually sufficient.

Metabolic alkalosis (pH>7.45, HCO_3^->30 mEq/liter)
- o Is the result of an increase in plasma $[HCO_3^-]$.
  - – An increase in $[HCO_3^-]$ of 10 mEq/liter increases pH by 0.15.
- o Is a consequence of the loss or sequestration of gastric contents (H^+ loss), the administration of diuretic drugs (K^+ loss), and, less frequently, excessive sodium bicarbonate administration.
- o *Treatment* is aimed at removing the underlying cause, such as H^+ losses via gastric reflux.

II. Physicochemical approach

Henry Stämpfli

- Also known as the 'electrolytes and protein included' approach.
- Details of mathematical relationship and interdependence of $[H^+]$ ions with electrolytes, CO_2 and proteins may be viewed in the textbook *How to Understand Acid–Base* by Peter Stewart (Elsevier, New York), which is available free online at http://www.acidbase.org/index.php?show=sb.

A. Brief review of physicochemistry and definitions

- ○ Many substances (e.g. NaCl) when dissolved in water dissociate into charged molecules called *ions*, through a chemical process in which the molecular identity of the original added molecules change.
- ○ These formed ions are called *electrolytes* and it is convenient to subdivide them into *strong* and *weak* electrolytes.

Strong electrolytes

- ○ Strong electrolytes are fully dissociated and the main ones involved in acid–base balance are Na^+, K^+, Cl^-, Mg^{2+}, SO_4^{2-}, Ca^{2+}, and a few organic acid anions, notably L-lactate.
- ○ A major feature of these ions is their electrical charge and the preferred unit is equivalent per liter (Eq/liter).
  - – For *univalent electrolytes*, concentration in equivalents per liter is identical to the concentration in moles/liter.
  - – For *n valent electrolytes*, concentration is *n* times the concentration in moles/liter.
- ○ It is the strong electrolyte component (e.g. Na^+ component in the bicarbonate solution) in the solution that determines acid–base changes in the target patient, not the anion HCO_3^- as is often emphasized in textbooks.

Weak electrolytes

- ○ Weak electrolytes (e.g. plasma proteins) are substances that only partially dissociate when dissolved in water. Molecules of the parent substance, as well as the products of dissociation, exist together in solution.
- ○ These molecules are always in the dissociation equilibrium according to their dissociation constant K_A.
- ○ Weak electrolytes change their degree of dissociation depending on the conditions.
- ○ The amount of each component substance in any aqueous solution remains constant unless one of the following occurs:
  - – A substance is added or removed from the solution.
  - – A substance is destroyed or generated by chemical reaction.
- ○ With regard to hydrogen ions, the latter is most important. This is the basis of *mass conservation*.

Strong ion difference

- ○ Quantitatively, it can be shown that the $[H^+]$ and the $[HCO_3^-]$ of watery solutions (e.g. blood, plasma and serum) directly depend on the partial pressure of CO_2, the total protein concentration (weak acid), and, most importantly, the concentrations of the fully dissociated electrolytes.
  - – Na^+, K^+, and Cl^- are particularly important in this regard, especially the difference between $(Na^+ + K^+)$ and Cl^-.
  - – This is called *strong ion difference* (SID).
- ○ A normal SID is 44, calculated by $(Na^+ + K^+) - Cl = (140 + 4) - 100 = 44$.
- ○ Change in SID is the main mechanism by which body fluids affect $[H^+]$.

Concept of the Gamblegram

o   Gamble developed a concept termed the 'Gamblegram', which shows electroneutrality semiquantitatively and visually demonstrates the proportional distribution of different cations and anions in an aqueous sample (see Fig. 7.1) and how solutions will correct or change acid–base balance in blood (see Fig. 7.2) and in the extracellular space.

o   The law of electroneutrality requires that the sum of all cations equals the sum of all anions at all times ($\sum$ anions = $\sum$ cations) and applies to watery biologic solutions (e.g. blood, plasma).
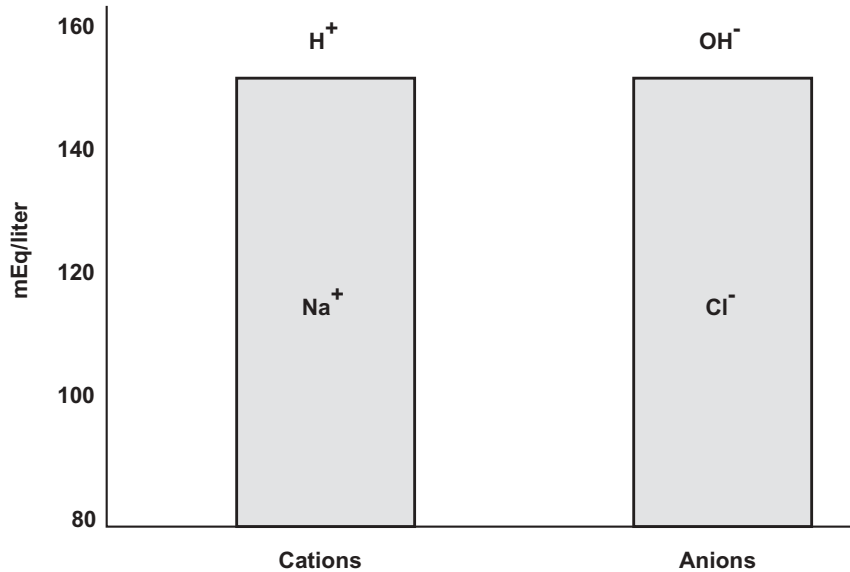
Fig. 7.1   A simplified Gamblegram of 0.9% saline.
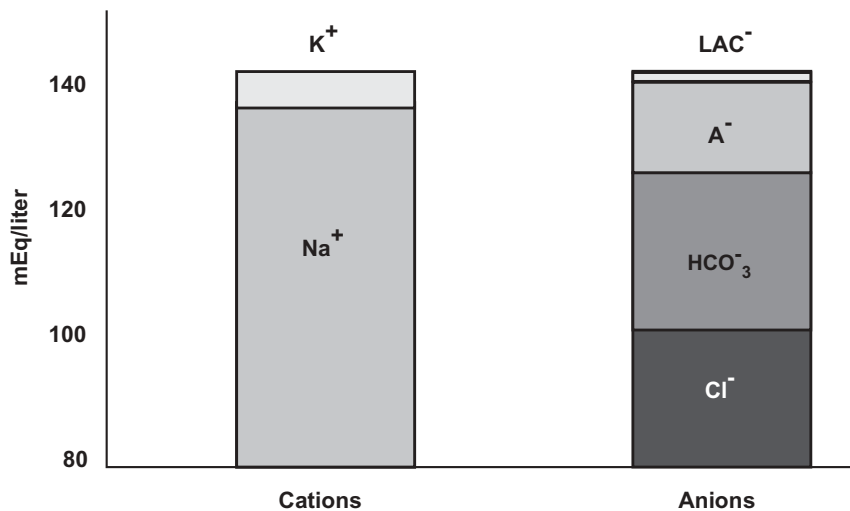
Fig. 7.2   A simplified Gamblegram of normal plasma.

- ○ An important consequence of this law is that addition of one single cation or anion to a watery solution is not possible; any aqueous solution is always electrically neutral.
    - – It follows that a patient cannot be treated parenterally (IV) with bicarbonate *alone*, as is often stated, since there will also always be a neutralizing cation (e.g. sodium).
- ○ A^- is the anion gap and represents the net negative charge on the weak acids of plasma, principally the serum proteins (especially albumin).
- ○ The parent substance of A^- is called A_{tot}. These species-specific normal A_{tot} values are now reported for horses and may be used for quantitative calculations using specific computer programs for physicochemical calculations.
- ○ Using the full Stewart equation, A^- can be precisely calculated. However, to figure the approximate concentration of A^- in mEq/liter, a Gamblegram may be utilized. When constructing Gamblegrams, the concentration of total protein in g/liter is multiplied by a factor of 0.175 (1.75 if the total protein is in g/dl).
    - – For example, in Fig. 7.2, $A^- = 12.5$ mEq/liter corresponding to a protein concentration of 71.4 g/liter (7.14 g/dl).
- ○ This information, along with a given bicarbonate value, may be used to calculate the non-protein unmeasured anions (strong ion gap).
    - – In Fig. 7.2, the value of the strong ion gap is 1.5 mEq/liter, which is attributable to L-lactate.
- ○ If all different variables of a system are properly measured and/or calculated, the electroneutrality equation can be used as a quality control.

B. Examples of metabolic abnormalities causing acid–base derangements

- ○ Most acute acid–base changes result from changes in strong ions.
- ○ The major driving forces for interactions between body fluid compartments are strong ion exchanges.

Dilutional acidosis

- ○ Changing the amount of free water will concentrate or dilute the electrolytes.
- ○ For example:
    - – 1 liter of simplified plasma *in vitro* contains 140 mEq/liter Na^+ and 100 mEq/liter Cl^- (SID = $140 - 100 = 40$ mEq/liter). A^- (the net charge on protein) will be about 14 mEq/liter, and HCO_3^- will be 26 mEq/liter (based on electroneutrality equation).
    - – If 1 liter of H_2O is added, the following concentrations result:
        Na^+ = 70 mEq/liter
        Cl^- = 50 mEq/liter (SID = 20 mEq/liter).
        A^- = 7 mEq/liter,
        HCO_3^- = 13 mEq/liter
    - – Clearly, a *metabolic acidosis* has resulted.
    - – Traditionally, without considering the electrolytes, this would be explained as a dilutional acidosis because $[HCO_3^-]$ is diluted (decreased). However, this cannot explain why the hydrogen ions are not diluted and have actually increased in concentration, clearly ignoring the dependency of $[H^+]$ concentrations on strong electrolytes (SID).

- o In an actual patient, the changes in SID will not be as dramatic as illustrated in this *in vitro* example. This is because parenteral treatment with electrolyte solutions is, in reality, a treatment of the plasma space plus the interstitial fluid space, which usually is four to five times larger than the plasma space.
- o Dilutional acidosis usually results in hyponatremia in *in vivo* situations, and often textbooks will state that this condition should be corrected with parenteral hypertonic saline. However, rapid infusion of 0.9% NaCl or NaCl (3–7%) will create a concurrent hyperchloremic metabolic acidosis.
  - – Thus, while the hyponatremia is corrected, the acidosis will worsen.
  - – Sodium bicarbonate may be a much better choice to correct the hyponatremia.

Contraction alkalosis
- o Occurs with fluid intake restriction or with diuretic treatment.
- o For example:
  - – 1 liter of simplified plasma (SID = 40 mEq/liter; Na^+ = 140 mEq/liter; Cl^- = 100 mEq/liter; A^- = 14 mEq/liter; HCO_3^- = 26 mEq/liter) loses half of its water.
  - – The following increases in concentrations of electrolytes, bicarbonate, and proteins result: SID = 80 mEq/liter; Na^+ = 280 mEq/liter; Cl^- = 200 mEq/liter; A^- = 28 mEq/liter; HCO_3^- = 52 mEq/liter.
  - – Clearly, a *metabolic alkalosis* results.
  - – Hydrogen ions have actually decreased in concentration, again showing the dependence on strong electrolytes.

Normal saline-induced acidosis
- o A well described outcome of rapid saline infusion.
- o For example:
  - – 1 liter of simplified plasma (SID = 40 mEq/liter; Na^+ = 140 mEq/liter; Cl^- = 100 mEq/liter; A^- = 14 mEq/liter; HCO_3^- = 26 mEq/liter) is mixed with 1 liter of 0.9% saline (SID = 0; Na^+ = 154 mEq/liter; Cl^- = 154 mEq/liter).
  - – The resulting SID of the 2 liter is 20 mEq/liter (Na^+ = 147 mEq/liter; Cl^- = 127 mEq/liter; A^- = 7 mEq/liter; HCO_3^- = 13 mEq/liter).
  - – The acid–base interpretation of this *in vitro* solution is a *hyperchloremic metabolic acidosis*.

Hypochloremic alkalosis
- o Chloride shifts occur in patients with gastrointestinal abnormalities (e.g. gastric reflux).
- o Resulting hypochloremia increases SID and, based on electroneutrality, the change will be balanced by an increase in HCO_3^- concentration.
- o Administration of 0.9% NaCl will be an effective treatment.
- o If concurrently *hypokalemic*, part of the saline may be replaced with KCl.

Hyperchloremic acidosis
- o Result is a decrease in SID.
- o Usual treatment is $NaHCO_3^-$ solution to normalize SID.
  - – Eventually renal handling of Cl^- will correct the hyperchloremia.
- o Sodium salts of lactate, gluconate, acetate, propionate, or citrate are also used.

Lactic acidosis
- ○ Production of lactate ions under hypoxic conditions is the most important ionic interaction between intracellular fluids (ICF) and extracellular fluids (ECF) that affects SID.
- ○ Lactate accumulation may result from increased production, reduced catabolism, or a combination of the two.
- ○ Lactic acidosis results in lower SID and, consequently, in increased $[H^+]$.

C. Clinical application

- ○ Clinical decisions regarding acid–base are usually based on plasma parameters including $[H^+]$ (from pH), PCO_2, and tCO_2 (calculated from pH and PCO_2 and expressed as $[HCO_3^-]$).
- ○ With multiparameter blood gas analyzers, $[Na^+]$, $[Cl^-]$, $[K^+]$ and $[lactate^-]$ SID are often available.
- ○ Once pH and PCO_2 are measured, and bicarbonate values and electroneutrality states are known, the following calculation can be done:
    $$[SID] - [HCO_3^-] - [A^-]$$
    - – If this is positive, an unmeasured strong anion must be present (strong ion gap), and usually this is L-lactate.
    - – If this is negative, there must be a measurement error.
- ○ The importance of bicarbonate:
    - – Changes in $[HCO_3^-]$ have to be understood in terms of changes in SID, PCO_2, and possibly A_{tot} just as $[H^+]$ changes do.
    - – $[HCO_3^-]$ is not relevant to the relationship between $[H^+]$, SID, PCO_2 and A_{tot}.
        - ■ This is because $[HCO_3^-]$ is never measured but always calculated.

8   Hemotherapy and hemostasis

Hemostasis

Casey J. LeBlanc

I. Normal physiology

- Normal hemostasis is the result of a compilation of physiologic processes that maintains blood in a fluid, clot-free state within normal vessels and induces a rapid and localized *plug* at the site of a vascular injury.
- The primary components that perform these processes are *platelets*, *coagulation factors*, *regulators of coagulation*, and the *vascular wall*.
- Under normal circumstances, *endothelial cells* maintain an environment conducive to liquid blood flow by numerous mechanisms that block platelet adhesion and aggregation, inhibit the coagulation cascade, and actively lyse blood clots.

II. Factors preventing excessive hemorrhage

- Significant hemorrhage is prevented by a general sequence of events that include:

A. Vasoconstriction

- Transient arteriolar vasoconstriction is largely attributable to reflex neurogenic mechanisms and augmented by the local secretion of factors such as *endothelin*.

B. Primary hemostasis

- Platelets adhere to exposed subendothelial structures, most importantly *collagen*, via *von Willebrand Factor* (vWF).
- Once adhered, platelets undergo shape change and release granule products, primarily *thromboxane A_2* (TXA$_2$) and *adenosine diphosphate* (ADP), which promote recruitment of additional platelets and the formation of a hemostatic *plug*.

C. Secondary hemostasis

- The platelet plug is substantially reinforced by a fibrin network resulting from activation of a series of proteolytic enzymes (see Fig. 8.1).
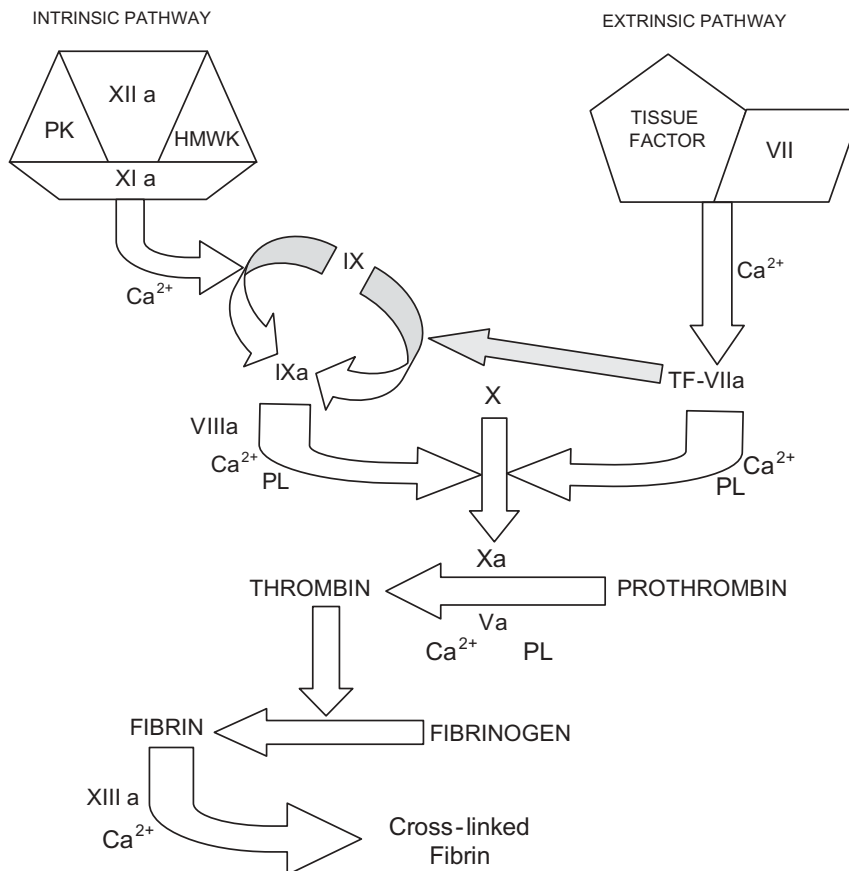
Fig. 8.1   Intrinsic and extrinsic pathways in clot formation.

   o Coagulation begins when blood contacts a negatively charged surface (e.g. sub-endothelial collagen), resulting in the absorption and activation of factor XII (*intrinsic pathway*).
      – Alternatively, tissue injury results in the release of tissue *thromboplastin* (tissue factor) and subsequent activation of factor VII (*extrinsic pathway*).
   o Initiation of either pathway results in the activation of factor X (*common pathway*), ensuring the formation of *thrombin*, *fibrin*, and an *insoluble fibrin clot*.
   o Although *in vivo* coagulation is undoubtedly more complex than portrayed in a classic Y-shaped diagram, the concept is beneficial when evaluating laboratory tests.

III. Inhibition of coagulation

- Once initiated, coagulation must be restricted to the site of vascular injury.
- Aside from limiting factor activation to sites of platelet phospholipid exposure, coagulation is also regulated by *antithrombins* (e.g. antithrombin III), *proteins C and S*, and *tissue factor pathway inhibitor* (TFPI).

IV. Fibrinolysis

- To maintain a patent blood vessel following vascular injury, degradation of fibrin is primarily mediated by the active enzyme *plasmin*.
- Plasmin results from the enzymatic breakdown of its precursor *plasminogen*, inducted by a factor XII-dependent pathway or two immunologically distinct plasminogen activators, *tissue plasminogen activator* (tPA) and *urokinase plasminogen activator* (uPA).
- The breakdown of fibrin and fibrinogen results in the formation of *fibrin(ogen) degradation products* (FDPs), also called *fibrin split products* (FSPs).

V. Tests of hemostasis

A. Platelet enumeration

- *Normal platelet concentration for horses is 1×10^5 to 6×10^5 platelets/μl.*
- Methods include the use of automated impedance or light scatter analyzers, hemocytometers, and estimation from a stained blood smear.
- An average of 6–10 platelets/100× (oil immersion field) is considered adequate.
- A *decreased* platelet concentration can result from (aside from thrombocytopenia), clotting of blood samples and *in vitro* platelet clumping.

B. Bleeding time

- Procedure should be reserved for use in horses with *adequate platelet concentration*, but *questionable platelet function*.
- This test is performed by puncturing a clipped area on the side of the neck or inside the lip with a manufactured template or an 18-gauge needle inserted to 4 mm.
- Accumulated blood should be removed with tissue paper, but the puncture site should not be disturbed.
- *Normal bleeding times are 2–6 min.*

C. Antiplatelet antibody

- Numerous tests have been developed to detect antibodies or antigen–antibody complexes on platelets or megakaryocytes as the cause of primary or secondary immune-mediated thrombocytopenia.
- Flow cytometric detection of platelet-bound IgG and IgM using species-specific, fluorescently labeled antibodies is a very sensitive assay performed with increased frequency in specialized laboratories.

D. Activated clotting time (ACT)

- A simple, inexpensive, point-of-care test of the intrinsic and common pathways.
- Platelets provide the phospholipid surface for coagulation to occur; therefore, severe thrombocytopenia ($<10^4$ platelets/μl) may prolong ACT.
- Blood (2 ml) is drawn into a pre-warmed (37°C) vacuum tube containing a contact activator (diatomaceous earth).

    ○ *Normal ACT for horses is 163 ±18 seconds.*
    ○ ACT is the time from contact of blood with the activator to the initial sign of a clot.
    ○ Factor activity must be ≤5% of normal to *prolong* ACT; therefore, ACT is a *less sensitive* test than an aPTT (see below).

E. Activated partial thromboplastin time (aPTT)

    ○ Blood should be collected non-traumatically into 3.8% sodium citrate tubes at a blood:anticoagulant ratio of 9:1.
    ○ *A normal aPTT for horses is 25−45 seconds.*
    ○ A *prolonged* aPTT indicates a coagulation factor deficiency in the intrinsic pathway (factors XII, XI, IX, and VIII) or common pathway (factors X, V, thrombin, and fibrinogen).
        – Factor activity must be <30% of normal to prolong aPTT.

F. Prothrombin time (PT)

    ○ Blood should be collected and submitted as described for aPTT.
    ○ PT measures the time required for fibrin clot formation to occur after the addition of tissue thromboplastin and calcium to citrated plasma.
    ○ *Normal PT for horses is 9.5–11.5 seconds.*
    ○ A *prolonged* PT indicates a coagulation factor deficiency in the extrinsic pathway (factor VII) or common pathway (factors X, V, thrombin, and fibrinogen).
        – Factor activity must be <30% of normal to prolong PT.

G. Fibrinogen (150−400 mg/dl)

    ○ Methods of measurement include:
        – Heat precipitation (simplest method, but not suitable for detecting hypofibrinogenemia).
        – Modified *thrombin time* (TT) measures time for conversion of fibrinogen to fibrin.
        – Immunologic assays.
    ○ Fibrinogen is also an acute phase protein and its hepatic synthesis is commonly increased in inflammatory conditions.
    ○ Despite normal or high plasma fibrinogen concentrations with coagulopathies, TT can be prolonged due to the presence of thrombin inhibitors (e.g. heparin, fibrinogen degradation products).
        – In disseminated intravascular coagulation, plasma fibrinogen concentrations tend to be normal or increased.

H. Fibrin(ogen) degradation products (FDPs)

    ○ *Normal FDP concentration is <10 μg/ml.*
    ○ FDPs are usually detected utilizing a latex agglutination assay.
    ○ Samples must be collected in specialized tubes containing thrombin or snake venom and soybean trypsin inhibitor (inhibits *in vitro* fibrinolysis).

- ○ *Increased* FDP concentrations usually indicate increased fibrinolytic activity; causes include DIC, deep vein thrombosis, significant internal hemorrhage, and severe liver disease (decreased FDP clearance), and physiologic or appropriate fibrinolysis.

I. D-dimer

- ○ *Normal D-dimer concentration is 0 or negative.*
- ○ Immunoturbidometric and latex-agglutination techniques are used to detect D-dimers in citrated plasma (few kits have been validated for horses).
- ○ Kits utilize monoclonal antibodies against specific fragments generated by plasmin degradation of cross-linked fibrin, as opposed to FDPs that are composed of fibrin and fibrinogen fragments.
- ○ D-dimer assays are typically more sensitive than assays used to detect FDPs.

J. Antithrombin

- ○ Commonly known as antithrombin III or ATIII.
- ○ *Normal plasma ATIII activity in horses is high compared with many species and ranges from ~218 ± 18% activity of normal human plasma or ~ 80–125% activity of pooled reference equine plasma.*
- ○ ATIII is the major physiological inhibitor of thrombin and factor X.
- ○ ATIII activity *decreases* with disorders such as DIC, protein-losing enteropathy or nephropathy, liver dysfunction, or ischemic/strangulating gastrointestinal lesions (associated with loss of ATIII into peritoneal cavity).
- ○ Heparin therapy accelerates the use and clearance of ATIII, leading to decreased plasma activity.
- ○ Age and breed differences in ATIII activity have also been identified.

VI. Hemostatic abnormalities (see Table 8.1)

Table 8.1   Results of typical hemostasis assays.

Disorder	Platelet count	Bleeding time	aPTT/ACT	PT	Fibrinogen	FDP/D-dimer
Thrombocytopenia	↓	↑	N*	N	N	N
Platelet function defect	N	↑	N	N	N	N
DIC	↓	↑	↑	↑	↓ or N or ↑	↑
Liver disease	N	N or ↑**	N or ↑	N or ↑	N	N or ↑
Intrinsic factor deficiency	N	N	↑	N	N	N
Vitamin K antagonism	N	N	↑	↑	N	N or ↑

* Severe thrombocytopenia (< 10^4 platelets/µl) can result in a mildly prolonged ACT but would have no effect on a PTT.

** Bleeding time may be prolonged if FDPs are present and coating platelets, resulting in decreased platelet adhesion.

A. Platelets

Congenital abnormalities
- o von Willebrand's Disease (vWD)
  - – Rare, but inherited vWD (Type II) has been reported in horses.
  - – Technically not a platelet disorder, but associated with decreased platelet adhesion to subendothelium.
- o Thrombasthenia
  - – Rare. Characterized by bleeding diathesis in the absence of thrombocytopenia, vWD, and a coagulopathy.

Acquired abnormalities
- o Thrombocytopenia. Spontaneous hemorrhage secondary to thrombocytopenia is possible with platelet counts $< 2 \times 10^4/\mu l$ and more likely if counts are $\leq 10^4/\mu l$.
  - – *Decreased production*. Secondary to toxin- or drug-induced marrow damage, neoplastic diseases, infectious agents (equine infectious anemia virus), or immune-mediated damage.
  - – *Increased consumption/utilization* (e.g. DIC, and disseminated neoplasia).
  - – *Increased destruction*. Usually associated with an immune-mediated mechanism that may be primary (immune-mediated thrombocytopenia or ITP) or secondary to a long list of other diseases and drugs.
  - – *Sequestration*. Marked splenic congestion or neoplasia may cause mild thrombocytopenia.
  - – *Platelet defects*. Acquired functional disorders such as decreased platelet adhesion or aggregation have been associated with the use of certain drugs and diseases.

B. Coagulation defects

Congenital factor defects
- o Rare.
- o Cases are intrinsic factor deficiencies and therefore cause a prolonged aPTT only.

Acquired factor defects
- o DIC
  - – A pathologic activation of the coagulation system resulting in inappropriate hypercoagulation and secondary hemorrhage throughout the circulatory system.
  - – Common syndrome secondary to many disease states in the horse including acute gastrointestinal diseases, laminitis, sepsis, and disseminated neoplasia.
- o Vitamin K antagonism.
  - – A feature of rodenticide toxicity. (Occurs rarely in horses.)

Therapy induced
- o ε-Aminocaproic acid, a lysine analog that inhibits fibrinolysis, has been associated with mildly decreased fibrinogen concentration and aPTT in normal horses.
- o Hydroxyethyl starch (Hetastarch®) has been associated with a reduction in vWF:Ag activity, decreased FVIII:C activity, but a shortening of both aPTT and PT.
- o Heparin (especially unfractioned) is associated with prolongation of aPTT, TT, and potentially PT in normal horses and horses with colic.

Hemotherapy

Hanna-Maaria Palos

I. Introduction

A. Transfusion

- o Defined as intravenous therapy with blood or blood products.
- o Indications include anemia, coagulopathy or immunodeficiency.
  - – The most common indications for transfusions in anesthetized horses are acute blood loss (whole blood transfusion) and intestinal surgery (plasma transfusion).

B. Anemia

- o Refers to decreased oxygen carrying capacity of blood.
- o The 'transfusion trigger' (the point at which to transfuse) in anemia depends on whether anemia is acute or chronic.
- o In acute blood loss, all the components of the blood are lost and treatment with *whole blood* is logical.
- o In euvolemic anemia, only the red blood cells (RBCs) are lost, and treatment with *RBCs* is logical.

C. Oxygen carrying capacity

- o Is primarily a function of RBCs.
- o A small amount of oxygen is carried in the dissolved state in the plasma.

D. Oxygen delivery (DO$_2$)

- o Is a function not only of RBCs (hemoglobin saturation) but also of blood flow (cardiac output).

$$DO_2 \text{ (ml/min)} = CaO_2 \times \text{Cardiac output (liters/min)}$$
$$= \left(1.36 \times Hb(mg/dl) \times \frac{Hb \text{ \%Sat}}{100} \right) + (0.003 \times PaO_2) \times \text{Cardiac output (liters/min)}$$

(1.36 = ml O$_2$ carried by 1 g Hb; 0.003 = solubility coefficient of O$_2$ in blood)

E. Acute blood loss

- o The decrease in cardiac output and RBC count is jointly responsible for the overall decrease in O$_2$ delivery.
- o Improving cardiac output (IV fluid therapy) is sufficient to restore O$_2$ delivery to acceptable values in many cases of acute blood loss.

F. Chronic anemia

o Blood volume may be normal; however, the decrease in RBCs may result in a decrease in O_2 delivery.
o This may be offset somewhat by the reduction in viscosity associated with decreased RBC mass which favors blood flow and hence O_2 delivery. Consequently, there may not be signs of distress at rest.

G. Blood volume (liters)

o In the adult horse, blood volume is approximately 70–80 ml/kg body weight.
 – Volume may be closer to 100 ml/kg in a fit Thoroughbred.
o It depends on factors such as age, body type and level of fitness.

H. RBC antigens

o Horses have several RBC type antigens.
o Types Aa and Qa are the most relevant clinically.

II. Transfusions in acute blood loss

A. Immediate goals

o Control hemorrhage.
o Optimize preload.

B. Optimizing preload

o Restore the circulating intravascular volume with a bolus of fluids.
 – Fluids may be *isotonic* or *hypertonic* crystalloids and/or *colloids*.
 – However, administering hypertonic fluids in the presence of uncontrollable *bleeding into a cavity* may potentiate intravascular volume loss, due to the increase in osmotic pressure in the cavity.
o Inotropic (e.g. dobutamine) support is sometimes necessary.
o Vasopressors (e.g. phenylephrine) are warranted in some cases.

C. Massive blood loss

o A transfusion may be inevitable.
o The blood product of choice is fresh whole blood to replace all the components lost.
o The 'transfusion trigger' should be assessed for each case, but *as a general rule transfusion may be necessary at or after the loss of 30% blood volume*.
o It may be difficult to assess the degree of blood loss in an anesthetized horse. For example, anesthetized horses may not respond to blood loss with an increase in heart rate. However, a significant decrease in blood pressure is expected with major blood loss.

- o It takes time before the PCV changes after acute blood loss. This delay is dependent on whether replacement fluids are administered and the degree of internal fluid shifts.
- o It is important to measure, or reliably estimate, the amount of blood loss. This can be done by measuring the volume in the suction bottle (subtract the volume of saline flush) and weighing blood-soaked gauzes.
- o Central venous blood pressure (CVP) is an indirect method to evaluate circulating intravascular volume.
  - – If blood loss is anticipated, placing a CVP line prior to surgery is helpful in tracking trends.
  - – A rapidly decreasing CVP is an indication of massive bleeding.

III. Transfusions in euvolemic anemia

A. Chronic anemia

- o Chronic anemia often leads to some degree of physiological adaptation.
- o If chronic anemia causes clinical signs of compromised tissue oxygenation (e.g. tachycardia, weak pulses, increased respiratory rate, decreased exercise tolerance, and/or CNS depression), that is an indication to transfuse prior to anesthesia.
- o Because patients with chronic anemia are usually euvolemic, the blood product of choice is *packed red blood cells*, to avoid volume overload.

B. Hemolytic anemia

- o If a horse with hemolytic anemia needs to be anesthetized, there may be an indication to *transfuse prior to induction* of anesthesia.
- o A transfusion trigger has to be established case by case.
  - – As with chronic anemia, the presence of clinical signs is a strong indication for transfusion.
  - – A transfusion should also be considered if the PCV is < 20 or rapidly decreasing.
- o Horses with hemolytic anemia are usually euvolemic; so *packed red blood cells* are the blood products of choice.
  - – Packed red blood cells can be processed from anticoagulated fresh whole blood by centrifuging or allowing the cells to form a sediment. The plasma can then be separated and the cells transfused.

IV. Technical considerations when transfusing

A. Blood donor

- o Should be clinically healthy.
  - – Equine viral arteritis (EVA) negative.
- o Medium to large size.
- o Never been a recipient of a transfusion.
- o Geldings or unbred mares are better choices, because there is a low incidence of naturally occurring alloantibodies.
  - – Pregnancy sensitizes mares to RBC antigens.

- ○ *Preferably, the donor and recipient should be blood typed, and cross-matched.*
  - – This is not feasible in all cases.
  - – In most cases, a cross-match *negative for agglutination and hemolysis* is adequate.
- ○ A 'universal donor' is the second best choice.
  - – Aa- and Qa-negative horses negative for alloantibodies may be considered 'universal donors'.
- ○ In an *emergency situation*, in the absence of cross-matching or access to a 'universal donor', a gelding (preferably of the same breed as the recipient) is the best choice for donor.
- ○ A donor can donate up to 20 ml/kg of blood, or 10–15 ml/kg of plasma every 3 weeks.

B. Cross-matching

- ○ To test the compatibility of the donor and recipient, a cross-match should be performed whenever possible, especially if the recipient has a history of *transfusions* or *pregnancy*.
- ○ Washed cells are tested against plasma for *agglutination*. Blood cells contain the blood type *antigens*, and plasma may contain the *antibodies* against blood type antigens.
- ○ In a *minor cross-match*, recipient cells are tested against donor plasma.
- ○ In a *major cross-match*, donor cells are tested against recipient plasma.
- ○ To test for *hemolysins*, complement is added and the sample incubated.
- ○ The major and minor cross-match should be *negative for agglutination and hemolysis*.

C. Blood collection and storage

- ○ Fresh whole blood can be stored at room temperature for a few hours.
- ○ If blood is not going to be transfused within 4 hours, it should be stored in a refrigerator at 4°C. The shelf-life of stored equine blood has yet to be established.
- ○ Blood should always be collected aseptically into sterile anti-coagulated *collection bags.*
  - – Collecting blood into glass bottles is less desirable than using collection bags. Storing blood in glass inactivates the platelets, and the vacuum used for collection causes cell damage.

D. Preferred anticoagulants

- ○ CPDA-1 (citrate–phosphate–dextrose–adenine) and CPD (citrate–phosphate–dextrose).
  - – CPD = Na citrate 1.66 g, citric acid 188 mg, Na phosphate 140 g, dextrose 1.61 g in 63 ml; with 450 ml of blood added.
  - – CPDA-1 = Na citrate 1.66 g, citric acid 188 mg, Na phosphate 140 g, dextrose 2.0 g, adenine 17.3 mg in 63 ml; with 450 ml of blood added.
  - – These solutions contain preservatives and nutrients and are suitable for storage.
  - – CPDA-1 solution is optimal for storing equine blood.
- ○ Sodium citrate is the most commonly used anticoagulant for *immediate* transfusions in adult horses.
  - – 1 ml of 3.8% Na citrate per 9 ml of blood; i.e. 10% of final volume.

E. Storage lesions

o   Blood develops storage lesions over time.
o   The type and degree of lesion depend on the anticoagulant preservative media and the duration of storage.
o   Whether these lesions are clinically relevant depends on the health status of the recipient and the volume of blood transfused.
o   In the critically ill, neonates, patients with renal or hepatic impairment, or whenever massive volumes of blood are transfused, it is best to use fresh blood.

F. Examples of storage lesions

o   Platelets are not functional after refrigeration.
o   Labile coagulation factors (V, VIII, vWF) degrade.
o   The pH decreases *in vitro* due to acidic anticoagulant, and lactic acid build-up from RBC metabolism. However, *in vivo* post-transfusion metabolic alkalosis may occur (citrate is a substrate for bicarbonate).
o   The number of microaggregates increases.
o   RBC osmotic fragility increases.
  –   Loss of deformability, resulting in limited ability to pass through capillaries, results in increased adhesion to endothelium.
o   The concentration of 2,3-diphosphoglycerate (2,3-DPG) decreases, resulting in a left shift of the O_2 dissociation curve.
  –   The affinity of hemoglobin for O_2 increases, and offloading of O_2 to the tissues decreases. This may contribute to tissue hypoxia.
  –   The decrease of 2,3-DPG concentration is transient; however, it may take up to 24 hours to return to normal concentrations.
o   Increase in the concentrations of potassium and ammonium.
o   Increase in bioactive substances (e.g. cytokines, histamine, lipids).

G. Transfusion procedure checklist

o   Compatibility (e.g. blood typing, cross-matching, or 'universal donor').
o   Check label of stored blood. Do not use outdated or inadequately labeled blood products.
o   Visually inspect the blood. Clots or discoloration in stored blood may be due to bacterial growth. Such products have to be discarded.
o   Equipment needed: transfusion set with a filter.
o   Refrigerated blood may be warmed in a waterbath to room temperature or slightly above immediately prior to transfusion.
  –   Warming is important if the patient (e.g. neonate) is at risk of hypothermia.
  –   The temperature of the water should *not* exceed body temperature.
  –   Warming a blood product to higher than body temperature has to be avoided, as this leads to protein denaturation and cell damage.
o   A jugular catheter should be reserved exclusively for the administration of blood or blood products.
  –   Blood products should *not* be administered in the same line as calcium-containing solutions as this may lead to coagulation.

H. Dose and rate of transfusion

o   Depends on the patient and specific indications.

Whole blood transfusion

o   Blood volume required = Blood volume of recipient $\times \dfrac{\text{PCV increase desired}}{\text{PCV of donor}}$

–   *Example*:   Recipient (500 kg); PCV = 20%; Target PCV = 30%;
Donor PCV = 45%.

Desired increase in PCV	= 30 – 20
	= 10
Blood volume of recipient	= 8% of 500 kg
	= 40 liters
Blood volume to be transfused	= 40 liters × 10/45
	= **8.9 liters**

Packed red cell transfusion

o   Using packed red cells the volume required is less than when using whole blood.
o   The PCV of packed red blood cells could be as high as 70–80%.

–   *Example*:   Recipient (500 kg); PCV = 20%; Target PCV = 30%;
Packed red blood cell PCV = 70%.

Desired increase in PCV	= 10
Blood volume of recipient	= 40 liters
Volume of packed cells	= 40 liters × 10/70
	= **5.7 liters**

o   *Euvolemic patients* should be transfused at a slow rate to avoid volume overload.
o   In *acute bleeding*, transfusing approximately half of the blood volume deficit may be adequate. A balanced electrolyte solution may be used simultaneously to restore intravascular volume.
o   *Massive bleeding* may require a rapid transfusion rate.
o   Start transfusion slowly, unless massive ongoing bleeding is occurring.
o   Monitor for transfusion reactions.
–   If no reactions after 10–15 minutes, the rate may be increased.
–   Rates as high as 20 ml/kg/h (whole blood), or 10 ml/kg/h (packed red cells) have been recommended.
–   However, slower infusion rates (e.g. 5 ml/kg/h for whole blood and 2.5 ml/kg/h for packed red cells) reduce the risk of volume overload.

V. Considerations with allogenic blood transfusions

●   Despite efforts to make transfusion therapy safer, there will always be a risk involved.
●   Therefore, transfusions should be kept to a minimum.

A. Risk/benefit ratio

- In addition to cost/benefit ratio, the *risk/benefit ratio* should be considered before each transfusion.
- Transfused equine red blood cells survive only a few days, so, at best, a transfusion results in only a short-term improvement in oxygen carrying capacity.
- Even minor incompatibilities lead to further shortening of the lifespan of the transfused cells, emphasizing the importance of cross-matching.

B. Adverse effects

Adverse effects must be diagnosed promptly and treated, when possible. They include:
- Immunological transfusion reactions.
- Non-immunological transfusion reactions.
- Transmission of diseases.
- Immunomodulation/suppression.
- Severe transfusion reactions including:
  – Acute *hemolytic* transfusion reaction.
  – *Anaphylactic shock*.
  – *Hypotension*, due to vasodilation, is the most obvious sign during anesthesia.

Treatment
- Cessation of transfusion.
- Cardiovascular support (fluids ± epinephrine).
- Corticosteroids and antihistamines.
- In acute hemolytic transfusion reaction, it is also important to monitor and support kidney function and urine output.

VI. Alternatives to allogenic blood transfusion

A. Blood conservation

Includes all available strategies to reduce patient exposure to allogenic blood products including:
- Keeping blood loss to a minimum with optimal positioning of the patient (surgical site above the level of right atrium, although this may result in increased risk of air emboli).
- Use of minimally invasive surgical techniques.
- Rerouting blood from the surgical site by tourniquet or vasoconstriction (*epinephrine*), and avoiding inappropriately high central and peripheral venous pressures.

B. Autologous transfusion and hemodilution

- In both cases, the recipient acts as the donor.
- Donor should not be anemic.

Autologous transfusion
- ○ Is an option if blood loss during elective surgery is predicted.
- ○ Autologous donation is performed 1–3 weeks before surgery, giving the bone marrow time to regenerate cells.

Hemodilution
- ○ Is the technique of collecting blood immediately prior to or during anesthesia.
- ○ Blood is generally replaced with isotonic crystalloids ($3 \times$ the shed blood volume).
- ○ Has the advantage of not having to store the blood.
- ○ The blood lost during surgery has fewer RBCs per unit volume.

C. Red blood cell salvage

- ○ May be useful if there is massive bleeding.
- ○ Shed blood can be collected for autotransfusion with a 60 ml syringe and sterile IV tubing, or suction tip, peritoneal catheter or large pore tube, and a sterile collection bottle or a commercial kit.
- ○ Anticoagulant should be added.
- ○ Shed red blood cells should have normal function and survival and may have greater oxygen carrying capacity than stored blood.
- ○ However, coagulation and fibrinolysis is initiated, and platelets are activated during bleeding.
- ○ Thus, *shed blood does not support hemostasis*, and may contain microthrombi and increased concentrations of cytokines.

VII. Hemoglobin-based oxygen carrier solutions

- Oxyglobin® has been commercially available.
- Approved for dogs at a dose of 30 ml/kg.
- Used in horses at 5–15 ml/kg.
- Duration of effect approximately 18 hours.
- High oncotic pressure.
- Nitric oxide (NO) scavenger, thus may cause vasoconstriction.

VIII. Plasma transfusions

- Plasma contains water, albumin, coagulation factors, anticoagulation factors, and antibodies.
- Accepted indications for a plasma transfusion include:
  - ○ Coagulopathies (including DIC).
  - ○ Immunodeficiency (e.g. failure of passive transfer in neonate).
- The use of plasma for volume expansion, oncotic pressure support, and treatment of hypoalbuminemia is controversial, because there may be safer and more effective treatment options (e.g. Hetastarch).

- Plasma can be processed from anticoagulated fresh whole blood by letting the cells form a sediment, or by using a centrifuge.
  - Plasma can also be harvested from a donor via plasma apheresis.
  - Hyperimmune plasma can be acquired from commercial distributors.
- Once collected, plasma can be frozen and stored at −20°C or, ideally, colder.
  - All the coagulation factors are preserved for the first year of storage, and the product is called *fresh frozen* plasma.
  - After this time, the product is called *frozen* plasma.
  - For optimal IgG concentration, plasma should be used within 18 months of collection.
- Plasma should be thawed slowly in a warm water bath.
  - To avoid protein denaturation the temperature of the water should not exceed body temperature.
- Plasma should be transfused within 4 hours of thawing.
- Dose: approximately 10–20 ml/kg.
- The approximate dose required, can be calculated according to the following example:

  - *Example*: Plasma to treat hypoalbuminemia.
    Recipient (500 kg); PCV = 40%; Albumin = 1.5 gr/dl;
    Target albumin   = 2.5 gr/dl.
    Estimated blood volume   = 8% of 500 kg
                             = 40 liters
    Estimated plasma volume = (1 − PCV) × blood volume
                             = (1 − 0.4) × 40 liters
                             = 24 liters
    Note: Can also estimate plasma volume as ~ 5% of 500 Kg = 25 liters.

    $$\text{Vol. to be transfused} = \text{Recipient plasma vol.} \times \frac{\text{[Albumin] increase desired}}{\text{[Albumin] of the donor}}$$

    = 24 liters × 1/3.5
    = **6.9 liters**

- Infusion rates as high as 10–20 ml/kg/h have been recommended. However, a rate of 2.5–5 ml/kg/h may minimize the risk of volume overload.

9 The stress response

Deborah Gaon

- Anesthesia, surgery and trauma cause hormonal, physiological and metabolic changes recognized as the stress response.
- The purpose of stress is to restore homeostasis; however, the duration of the stress and physical condition of the patient can influence whether the stress response is beneficial or harmful.
- Generally, the magnitude of the stress response is related to the degree of trauma or the invasiveness of the surgery.
- Although a direct relationship between the stress response and surgical outcome has not been demonstrated, understanding how anesthesia and surgery activate the stress response can guide the anesthetist in minimizing its adverse effects.

I. Hormonal changes with the stress response

A. Catecholamines

- o Are released acutely in response to stress.
- o Increased secretion of epinephrine from adrenal medulla.
- o Increased secretion of norepinephrine from presynaptic, adrenergic nerve terminals.

B. Corticotropin releasing hormone (CRH)

- o Increased CRH from the hypothalamus stimulates pituitary pro-opiomelanocortin which is metabolized to ACTH and β endorphin.
- o ACTH stimulates the adrenal cortex to secrete cortisol.

C. Gonadotrophin releasing hormone (GnRH) and thyrotropin releasing hormone (TRH)

- o Decreased hypothalamic release of GnRH and thyrotropin releasing hormone (TRH) causes a decrease in the secretion of LH and FSH (pituitary gonadotrophins) and thyroid stimulating hormone (TSH).
- o Persistence of stress can lead to a decrease in metabolic and reproductive functions.

D. Insulin and glucagon

- o Insulin initially undergoes a mild, transient decrease.
- o Glucagon undergoes a transient increase.

E. Arginine vasopressin (AVP) and renin

- ○ Activation of these hormones is generally only associated with blood loss.
  - – Blood loss increases AVP release from the posterior pituitary and renin from the juxtaglomerular apparatus.
- ○ AVP also stimulates adrenocorticotropic hormone (ACTH) release from the pituitary.

F. Cytokines

- ○ Are not traditional hormones, but are locally produced low molecular weight proteins released from activated monocytes, fibroblasts, and endothelial cells following tissue injury.
- ○ Can stimulate the pituitary adrenal axis.
- ○ IL-6 is the major cytokine produced in response to surgery, but TNFα and IL-1 are also produced (IL = interleukin).
- ○ IL-6 stimulates the synthesis of acute phase proteins by the liver.
  - – Acute phase proteins act as inflammatory mediators in scavenging and tissue repair.

II. Physiological changes with the stress response

A. Cardiovascular changes in the anesthetized horse

- ○ Increase in blood pressure due to vasoconstriction.
- ○ Increase in systemic vascular resistance.
- ○ Decrease in cardiac output may occur secondary to vasoconstriction.
- ○ Decrease in tissue perfusion as a consequence of vasoconstriction.
- ○ Heart rate is generally unchanged in the horse (in contrast to other species).

Comment: These changes are the result of catecholamine release.

B. Water and electrolyte balance

- ○ AVP causes water retention and decreases urine output.
- ○ Renin stimulates angiotensin II production which increases aldosterone release from the adrenal cortex.
  - – This results in sodium and water retention in the distal tubules.

C. Thermoregulation

- ○ IL-6 can produce fever.

D. Immune function

- ○ Prolonged, excessively high cortisol concentrations may cause immunosuppression.
- ○ IL-6 affects B and T lymphocyte production and maturation.

III. Metabolic changes with the stress response

A. Changes in carbohydrate metabolism

○ Hyperglycemia.
  – This is related to the transient increase in glucagon and a decrease in insulin, which is likely caused by epinephrine and cellular resistance to insulin.
○ Catecholamines and cortisol increase hepatic glucose production by stimulating hepatic gluconeogenesis and glycogenolysis.
○ Amino acids (e.g. alanine) are also used for glucose production.

B. Changes in protein metabolism

○ Accelerated protein breakdown.
○ Cortisol causes a rapid immobilization of amino acids which results in an increase in muscle catabolism and a decrease in protein synthesis.
○ IL-1 is locally involved in muscle catabolism.
○ There is selective synthesis of positive, acute-phase reactants (e.g. C-reactive protein and fibrinogen).
○ There is a decrease in the synthesis of negative, acute-phase reactants (e.g. albumin).

C. Changes in fat metabolism

○ Cortisol and catecholamines promote lipolysis.
○ Triglycerides are metabolized into glycerol and fatty acids.
○ Ketogenesis can result but is dependent on the degree of metabolism induced.

IV. Activation of the stress response

A. Perioperative pain and surgical stimuli

○ In the horse, abdominal pain and surgery activate the stress response.
  – General anesthesia does not abolish the ability of the hypothalamus to respond to noxious stimuli.

B. Inhalational anesthesia

○ In the horse, halothane anesthesia *even without surgery* activates the stress response.
  – This response can be attenuated with volume expansion and dobutamine.
○ Inhalational anesthesia and poor tissue perfusion associated with hypotension have been identified as factors initiating the stress response.
○ The MAC of volatile anesthetics needed to block the autonomic response to surgery (MAC_{BAR}) is significantly higher than the MAC.

C. Intravenous anesthesia

- ○ Total intravenous anesthesia (alpha$_2$ agonists and *ketamine*) causes less activation of the stress response than does inhalational anesthesia.
- ○ This results in a reduction in the degree of vasoconstriction and improves cardiac output and tissue perfusion during surgery.

V. Methods of modifying the surgical stress response

- Balanced regimens (e.g. TIVA with alpha$_2$ agonists and *ketamine*) decrease the cortisol and adrenergic response to surgery.
- Increasing tissue perfusion, by avoiding intraoperative hypotension and hypovolemia, is especially important in horses anesthetized with inhalants.
- Local or regional anesthesia, as an adjunct to general anesthesia, reduces the neural input of the stress response and prevents nociceptive signals from reaching the CNS.
- A continuous infusion of *butorphanol* decreases the cortisol response and shortens hospitalization in horses post-celiotomy, indicating that opioids may have a role in decreasing the stress response.

VI. Benefits of blocking the stress response

- The outcome of reducing the stress response has not been thoroughly investigated in the horse but the likely benefits include:
  - ○ More stable cardiovascular parameters.
  - ○ A decrease in the hyperglycemic response and muscle catabolism.
  - ○ Fewer postoperative complications and shorter recovery times from surgery.

10 Thermoregulation

Ralph C. Harvey

I. Maintenance of body temperature

- Among the endothermic species, regulation of body temperature is tightly controlled and maintained within a narrow range.
  - *Piloerection* increases the thermal barrier of warmed insulating air surrounding the body. This barrier helps reduce further heat loss.
  - *Shivering thermogenesis* is very effective in generating body heat.
    - Shivering may even occur during light anesthesia.
  - *Non-shivering thermogenesis* is the generation of body heat through *increased muscle tone*.
- Fluctuations outside the normal range signify significant disease or stressors beyond the limits of physiologic control.
- Pharmacologic derangement of thermoregulation occurs with sedation, tranquilization, and anesthesia.

II. Heat loss from the body

- Heat loss occurs by:
  - Radiation.
  - Convection.
  - Conduction.
  - Evaporation of moisture from the skin and respiratory tract.
  - Excretion of urine and feces.
- Most significant losses are normally by *radiation* and *evaporation*.
  - *Sweating* is a remarkably effective method for heat loss.
- In normal awake subjects, the relative contribution of each mechanism varies with *ambient temperature*, *humidity*, and *wind speed*.
- Although anesthetic-induced hypothermia is much more common than hyperthermia, disruption of the normal processes for heat loss may lead to abnormal increases in body temperature.

III. Effect of general anesthesia on thermoregulation

A. Anesthetics and heat balance

- ○ Anesthetics alter one or more of the three components of heat balance:
  - – The afferent pathway.
  - – The central control mechanism.
  - – The efferent responses.
- ○ General anesthetics, particularly volatile anesthetics, *reset the threshold* for thermoregulation, so that a broader range of body temperatures is tolerated without response.
- ○ Once a response *is* triggered, it may still be incapable of restoring normal body temperature.

B. Phases of heat loss

- ○ Three phases of heat loss are observed during general anesthesia:
  - – An *initial* and *precipitous* decrease in body temperature due to a redistribution of core body heat to the periphery.
  - – Thereafter, a *progressive linear* decrease in temperature continues.
  - – A *vasoconstrictive* response ameliorates the linear decrease in temperature. This thermoregulatory response partially further limits temperature decreases by reducing blood flow to peripheral tissues.

C. Anesthesia and core body temperature in the adult horse

- ○ In adult horses, core body temperature decreases at ~ 0.4°C/h.
- ○ This decrease can be ameliorated by the use of *forced air warming*.
  - – Forced warming is unlikely to be effective in *restoring* core temperature.
- ○ Recovery of horses on cold surfaces leads to significant heat loss.
- ○ *Rectal* temperature accurately reflects core temperature.

IV. Adverse effects of hypothermia

- Significant heat loss is more likely to be a problem in *foals* or *miniature* horses, but efforts should be directed at preventing heat loss in every horse.
- Hypothermia affects *coagulation*, causing impaired platelet function, decreased activity of the coagulation pathways, and increased fibrinolysis.
- A significant *stress response* is elicited by hypothermia.
  - ○ Moderate hypothermia, 35°C (95°F), triggers a two- to seven-fold increase in release of catecholamines, with resulting vasoconstriction, tachycardia and hypertension.
  - ○ More severe hypothermia, in the range of 30°C (86°F), is associated with increased risk of atrial fibrillation.
  - ○ Profound hypothermia, 24°C (75.2°F) to 28°C (82.4°F), induces refractory ventricular fibrillation and death.
- The morbidity associated with these stress responses typically occurs during the postoperative period, rather than during anesthesia and surgery.

A. Hypothermia and wound healing

o   Hypothermia may delay wound healing.
  –   Mild perioperative hypothermia is *not* a significant risk factor for postoperative wound infection.
o   The risk of infection increases with the magnitude of the hypothermia and can be attributed to:
  –   Impairment of macrophage function.
  –   Reduced tissue oxygen partial pressure secondary to vasoconstriction.
  –   Decreased collagen deposition.

B. Metabolic consequences of hypothermia

o   The catabolic postoperative stress response is increased.
o   This response can be reduced by taking measures to maintain normal body temperature.
  –   Heat conservation with normothermia reduces muscle protein breakdown in human geriatric patients undergoing major gastrointestinal surgery.

C. Changes in anesthetic dosing with hypothermia

o   Hypothermia decreases the MAC for general anesthetics.
  –   MAC decreases 5% per 1°C decrease in temperature.
  –   Hypothermia increases the solubility of volatile anesthetics in tissues.
o   There is likely to be a decrease in clearance of injectable anesthetics.

V. Prevention of body heat loss during anesthesia

●   Insulating, to control radiant and convective losses, may reduce heat loss.
  o   The choice of insulating material seems to be of little importance.
●   Reduce contact with cold surfaces and surgical scrub solutions.
●   Use of low fresh gas flows.
●   Use of re-breathing circuits.

VI. Strategies to maintain or restore body temperature

A. Active heating

o   Is especially important in *neonatal foals* but should also be performed in adult horses, especially those of small body mass, where practical.
o   Heating devices and strategies should be applied *early* in order to prevent hypothermia, while concurrently monitoring body temperature to prevent overheating.
o   *Active heating* can be performed, with acceptable safety, by use of:
  –   Warm air blankets (most effective method).
  –   Circulating warm water blankets.
  –   Radiant heat sources above the patient and surgical field (can lead to overheating).
  –   The use of warmed intravenous and irrigation fluids.

– Less practical methods include warming and humidifying inspired anesthetic gases and increasing operating room and recovery area ambient temperatures.

B. Safety concerns with active heating

- ○ *There is a risk of thermal injury with all active heating systems.*
- ○ Control and monitoring are of paramount importance in the use of any of the active heating systems.
- ○ Using a broad distribution of heat to avoid localized hot spots, tissue drying, and burning is important.
- ○ Temperature monitoring should be considered mandatory whenever active heating is used (especially in very small foals).
- ○ Radiant heat in surgical and recovery settings can overheat tissues.
- ○ Heated/humidified anesthetic gases may burn or dry the airway.

VII. Shivering

- Shivering may occur during light anesthesia.
- Shivering can range from very fine contractions to more generalized and intense contractions of the trunk or limbs.
- The most common scenario is the development of gross shivering during recovery.
- While shivering can be very effective in restoring body temperature, it substantially *increases metabolic oxygen consumption*.
  - ○ Studies indicate that postoperative shivering may increase metabolic rates by as much as 400%.
  - ○ This can result in an oxygen debt since there is often residual reduction in ventilation, residual pulmonary atelectasis, or other respiratory insufficiency during the immediate postoperative period.
  - ○ Even when there is a four-fold increase in minute ventilation, shivering patients (human) can have arterial hypoxemia and inadequate oxygen delivery to tissues.

VIII. Hyperthermia under anesthesia

- This is a rare occurrence in the adult horse but it may have severe consequences.
- The body temperature may rise above normal by three mechanisms:
  - ○ Decreased loss of body heat through increased insulation (unlikely).
  - ○ Excessive or poorly controlled exogenous heating, often in combination with increased insulation or other environmental factors.
  - ○ Increased metabolic production of heat, including: stress-related hyperthermia, increased muscle tone, resetting of thermoregulatory processes, and malignant hyperthermia or related syndromes.
- Malignant hyperthermia (MH) and hyperkalemic periodic paralysis (HYPP), though relatively rare, are potential causes of hyperthermia.
- Hyperthermia could arise in foals from intensive warming and insulation.

11 Pharmacology of drugs used in equine anesthesia

Definitions of anesthetic terms

Many of the definitions used in veterinary anesthesia are based on responses in humans and cannot be strictly applied to animals in all instances.

- **Tranquillizer:** Predominant action is relieving anxiety without causing major sedation.
- **Sedative:** A drug which relieves tension and anxiety thereby allowing sleep.
- **Hypnotic:** Hypnosis is a drug-induced sleep.
  - A hypnotic is a depressant of the central nervous system.
  - A hypnotic enables patients to sleep more easily or intensifies the depth of sleep.
  - In general, hypnotics have no anesthetic action.
  - Hypnotics will *not* induce sleep in the presence of severe *pain*.
- **Neurolept:** A major tranquillizer.
  - Includes *phenothiazines* and *butyrophenones*.
    - Alpha$_2$ agonists do not fit the pharmacological profile of neurolepts.
  - The *pharmacological profile* of a neurolept includes:
    - Inhibition of motor activity including spontaneous movement and learned responses.
    - Antagonism of *apomorphine*-induced vomiting.
    - Antagonism of amphetamine-induced arousal.
- **Neurolept analgesia:** Combination of a *neurolept* and an *analgesic* (usually an opioid).
  - Example: *xylazine + morphine*.
- **Dissociative anesthesia** (e.g. *ketamine* anesthesia)
  - *Ketamine* produces a state of *dissociative anesthesia*.
  - Dissociation is based on EEG findings of a dissociation of the thalamocortical (synchronous δ waves are present) and limbic (θ waves are evident) systems.
  - Dissociative anesthesia is characterized by:
    - Analgesia.
    - Amnesia.
    - Catalepsy.
- **Catalepsy:** An akinetic state with loss of orthostatic reflexes.
  - The patient appears paralyzed by motor and sensory failure.
  - Catalepsy is a component of 'dissociative anesthesia'.
- **Balanced anesthesia**
  - The components of balanced anesthesia include:
    - Sedation or sleep.
    - Muscle relaxation.
    - Analgesia.
    - Amnesia.
  - Two or more drugs are required to provide balanced anesthesia.

Phenothiazines

- Phenothiazines, although still used in equine anesthesia, have largely been replaced by alpha$_2$ agonists.
- *Acepromazine* is the most commonly used phenothiazine.
- *Acepromazine* does not have a potent tranquillizing effect but has a potent effect on MAC reduction.

I. Acepromazine and receptor activity

- Phenothiazines exert a variety of effects on the CNS.
- The predominant sites of action appear to be *extrapyramidal*, and involve the basal ganglia, limbic system and brain stem.
- The phenothiazines exert their central tranquillizing effect by blocking dopamine receptors.
  - There are seven subtypes of dopamine receptors in the CNS, but D$_1$ and D$_2$ subtypes are the most numerous and are mainly located in the basal ganglia.
  - Dopamine has an important role in motor activity. Activation of dopamine in the input nuclei causes an increase in excitatory impulses reaching the cortex.

II. Physiological effects of phenothiazines

- Mild tranquillizing effect.
- Anti-histaminic (decrease histamine release from mast cells).
- Anti-emetic effect (not relevant in the horse).
- Decrease gastrointestinal motility (transient).
  - Anti-spasmodic effect on intestinal tract.
- Cardiovascular actions.
  - Anti-arrhythmogenic.
  - Vasodilation resulting in hypotension (due to alpha$_1$ blockade).
  - Cardiac output is generally not decreased in a healthy, awake horse.
- Antipyretic effect.
- Penile paralysis (*a rare occurrence in stallions*) is a dose-dependent effect.
- Whether phenothiazines lower the seizure threshold is a matter of debate.
- Large doses may produce extrapyramidal effects, but this is a rare occurrence.

III. Clinical use of acepromazine

A. Standing restraint

  - Administered at doses of 0.02−0.05 mg/kg, IV.
    - Up to 0.1 mg/kg has been recommended for IM, but lower doses are advised.
  - Can only get reliable restraint in a small percentage of horses.
  - Increasing the dose does not produce a better effect.
  - Onset of effect is slow.
    - ~ 20 min following IV administration.

- ○ Lack of analgesic action limits its use to non-painful procedures.
- ○ For more reliable sedation, can combine with an opioid or alpha$_2$ agonist.

B. Premedication prior to general anesthesia

- ○ Use of *acepromazine* as part of the premedication process has been shown to have a beneficial effect on the outcome of general anesthesia. The reasons for this may be multifactorial.

Reduced risk of death intraoperatively
- ○ The exact reason is undetermined but it may be related to the following factors:
  - – Decreasing the MAC reduces the negative cardiovascular effects (arrhythmias, myocardial depression, cardiac arrest) of volatile anesthetics.
  - – *Afterload reduction* leading to a decrease in myocardial wall stress.

Improved recoveries
- ○ May simply be due to *acepromazine*'s tranquillizing effect, increasing the time before the first attempt to stand.
- ○ May result from the improved cardiovascular function of MAC reduction and consequent improvement in muscle perfusion, leading to improved muscle strength at standing.

MAC reduction
- ○ MAC is reduced by about 30%, and this effect lasts for a few hours.

C. In combination with etorphine for neurolept anesthesia

- ○ *Acepromazine with etorphine* constitutes Immobilon® which is primarily used for capture of wild animals but is also used as an anesthetic in horses.

D. Contraindications of acepromazine

- ○ Can cause penile prolapse in stallions. Although *rare*, the condition can lead to serious consequences if it persists for a few hours and is untreated.
  - – The onset of penile edema makes retraction of the penis difficult or impossible.
- ○ Hypovolemia is another contraindication, as *acepromazine* may cause severe hypotension in such cases.
- ○ *Acepromazine* is reported to be contraindicated in animals with seizures; however, this issue is still a matter of debate.

Alpha$_2$ adrenergic agents

- • Due to their sedating and analgesic effects, α_2 agonists are of great importance in equine anesthesia.
- • Alpha$_2$ receptors are present at diverse sites in the central and peripheral CNS, including brainstem nuclei (e.g. locus coeruleus), spinal cord laminae and sensory afferent terminals, and various organs.
- • Alpha$_2$ *antagonists* may be used to reverse the effects of α_2 agonists.

I. Alpha$_2$ subtypes

- Three different types of G protein-coupled receptor α_2 subtypes have been described.
- A fourth (α_{2D}) was thought to exist but now appears to be a variant of α_{2A}.
- Alpha$_2$ receptors are coupled to a number of signaling pathways.
- Catecholamine release from the central and sympathetic nervous system is thought to be regulated, presynaptically, by α_{2A}, α_{2B} and α_{2C} subtypes.

A. Alpha$_{2A}$ subtype

- Causes long-lasting hypotension.
- May also be involved in vasoconstriction.
- Controls norepinephrine release from sympathetic nerves.
- Regulates pain perception induced by systemic α_2 agonists.
- Responsible for sedative and anesthetic-sparing effects of α_2 agonists.
- Has anti-epileptogenic effect.
- Inhibits dopamine release in basal ganglia.
- Inhibits 5HT release in hippocampus and brain cortex.
- Inhibits insulin release by decreasing cAMP in pancreatic islet cells.

B. Alpha$_{2B}$ subtype

- Responsible for initial hypertension following systemic α_2 agonists.
- Mediates some antinociceptive actions of NO_2.
  - Activation of endorphin release in periaqueductal gray by NO_2 stimulates a descending pathway which releases norepinephrine and affects α_{2B} receptors in the dorsal horn.
- Appears to mediate some cardiovascular effects of *etomidate*.

C. Alpha$_{2C}$ subtype

- Functions are less well described.
- Thought to be involved in spinal antinociception.
- Controls epinephrine release from adrenal gland.
- Inhibits dopamine release in basal ganglia.
- Inhibits 5HT release in hippocampus and brain cortex.
- Inhibits insulin release, by cAMP-independent mechanism, in islet cells.
- Inhibits the processing of sensory information.

II. Physiological effects of α_2 agonists

- Sedation (α_{2A}).
- Decrease MAC of volatile anesthetics.
- Somatic and visceral analgesia (α_{2A}, α_{2B}).
- Initial hypertension (α_{2B}) is followed by hypotension (α_{2A}).
- Decreased cardiac output.

- o Increase systemic vascular resistance.
- o Decrease heart rate.
- Bradycardia – second-degree heart block (transient) is common.
  - o Increased vagal tone.
  - o Decreased sympathetic outflow.
- Respiratory depression with high doses.
- Increase urine output.
  - o Block vasopressin action on renal tubules.
  - o Increase release of atrial natriuretic peptide.
- Decreased gastrointestinal motility.
  - o Inhibition of acetylcholine release in myenteric plexus.
- Variable effect on gastric secretion.
- Hyperglycemia.
  - o Inhibit insulin release (α_{2A}) (α_{2C}).
- Growth hormone release enhanced.
- Uterine contraction in late pregnancy (does *not* seem to be a problem in mares).
- Decreased surgical stress response.
- Thermoregulation is affected and shivering is inhibited.
  - o Hypothermia usually a sequel.
  - o Hyperthermia may result if ambient temperature is high.
- Sweating (especially under the mane and forelock) is common.

III. Clinical use of α_2 agonists and antagonists

A. Alpha$_2$ agonists for standing sedation

- o Under α_2 agonist sedation the horse's head will become lowered, thus facilitating its ability to balance on the fore limbs and kick violently with both rear limbs. For this reason, the *head should be raised*, especially when examining the pelvic limbs.
- o Ataxia is dose-related, and is more severe with *detomidine* and *xylazine* than with *romifidine*.
- o Duration of action (equipotent doses): *romifidine > detomidine > xylazine*.
- o Alpha$_2$ agonists are the agents most widely used to produce standing sedation.
  - – Titrating these agents to effect can vary the degree of sedation.
  - – Degree and duration of sedation is dose- and drug-dependent.
  - – High doses of *detomidine/romifidine* increase *intensity* and *duration* of sedation.
  - – Sedation persists for many hours following high-dose *detomidine* (40–60 μg/kg).
- o The IM dose is 2–3 × the IV dose and takes 15–30 minutes for peak effect.
- o *Oral* or *buccal* absorption of *detomidine* (0.06 mg/kg) produces sedation in approximately 45 minutes.
  - – The drug will not be effective if swallowed.
- o Alpha$_2$ agonists may be combined with phenothiazines or opioids.
  - – Combinations of α_2 agonists with opioids (e.g. *morphine*) give more reliable sedation.
  - – The horse is also less likely to suddenly react to stimuli.
- o An *infusion* can be given if standing sedation of long duration is planned.
  - – Example: *detomidine* 0.6 μg/kg/min following a loading dose (7–8 μg/kg) will give heavy sedation and can be combined with opioids for painful procedures.

B. Sedation with α_2 agonists prior to general anesthesia

o The dose of α_2 agonists used prior to induction will depend greatly on the method of induction.

o If *ketamine* alone (2.2–2.5 mg/kg, IV) is used for induction following α_2 sedation, it is *critical* that the horse be heavily sedated (lowered head, droopy lip, wide-based stance) before administration. Otherwise, more α_2 agonist should be administered before giving *ketamine*.

Examples of dose rates

Xylazine	(1–1.5 mg/kg, IV)
Detomidine	(0.01–0.02 mg/kg, IV)
Romifidine	(0.08–0.12 mg/kg, IV)
Medetomidine	(0.005–0.007 mg/kg, IV)

o If *ketamine* is combined with a benzodiazepine (e.g. *diazepam* 0.05 mg/kg, IV) for induction, a lower dose of α_2 agonist may be used, if desired, as the benzodiazepine will provide additional sedation and muscle relaxation.

o If *ketamine* is combined with *guaiphenesin* for induction, muscle relaxation is improved, thus the dose of α_2 may be reduced.

C. Alpha$_2$ agonists to maintain anesthesia

o Infusions of α_2 agonists can be used in conjunction with other injectable agents, primarily *ketamine*, to maintain anesthesia. (See TIVA, Chapter 15.)

o They may also been used in conjunction with volatile anesthetics for this purpose. (See PIVA, Chapter 15.)

D. Epidural administration of α_2 agonists

o These agents can be administered epidurally, alone or with local anesthetics, to provide analgesia or as an adjunct to general anesthesia.

o Combination with a local anesthetic prolongs the duration of action. (See Chapter 17.)

E. Alpha$_2$ antagonists

o Are rarely indicated for reversal of α_2 agonist-induced sedation in horses.

o Exceptions include:
   – Cardiorespiratory compromise from overdose of α_2 agonists.
   – To shorten the prolonged sedation of high-dose *detomidine* or *romifidine*.

o *Yohimbine* (0.15–0.25 mg/kg, IV) has weak antagonist activity.

o *Atipamezole* (0.15 mg/kg, IV) has potent antagonist activity.

IV. Advantages of α_2 agonists

- Good analgesia.
- Dose-dependent sedation.
- Compatible with many anesthetic drugs.

- Decrease MAC of volatile agents.
- Block stress response.
- Can be given IV, IM, epidurally, buccally.
- Small volume.
- Reversible.

V. Disadvantages of α₂ agonists

- Cardiovascular effects.
  - ○ Arrhythmias.
  - ○ Decrease cardiac output.
  - ○ Hypotension.
- Decrease gastrointestinal motility.
- Diuresis.
- Decrease insulin release.
- Sedated horse may react to noise/stimuli.

Opioids

- Use of opioids alone for premedication has been controversial in the horse due to the inability of these drugs to cause sedation or reduce MAC.
- Opioids have a tendency to cause excitement or dysphoria at higher doses, especially if used without concurrent sedation.
- The recent realization that lower doses of *morphine* give better clinical results has renewed interest in its use in the horse.

I. Opioid receptors and mode of action

- Three different types of G protein-coupled opioid receptors have been described.
- Their main action is inhibitory and is primarily mediated by $G_i\alpha$ and $G_o\alpha$ types of G proteins.
- All receptors have the ability to induce analgesia despite having different pharmacological properties.

A. Mu (μ) receptors (OP3)

- ○ Are involved in a number of physiological actions at the spinal and supraspinal level.
- ○ Common opioids (*morphine*, *fentanyl*, *methadone*, *meperidine*) act at μ receptors.
- ○ Three subtypes of μ receptor have been characterized:
  - – μ_1 receptors mediate supraspinal and peripheral analgesia.
  - – μ_2 receptors mediate spinal analgesia and are responsible for respiratory depression and ileus.
  - – The third μ receptor mediates the actions of *morphine* metabolite M6G.

B. Kappa (κ) receptors (OP2)

- ○ Are involved in analgesia, sedation and CNS effects such as dysphoria.
- ○ Three subtypes of κ receptors have been proposed:
  - – κ_1 receptors:
    - ■ Are the sites of action of many mixed agonists–antagonists.
    - ■ Mediate supraspinal and spinal analgesia and sedation.
    - ■ Are responsible for CNS effects (e.g. dysphoria).
    - ■ Mediate diuresis.
  - – The pharmacology of κ_2 receptors is not well described.
  - – κ_3 receptors:
    - ■ Are believed to correspond to the *nalorphine* receptor.
    - ■ Are involved in supraspinal analgesia.

C. Delta (δ) receptors (OP1)

- ○ Are less well described.
- ○ Are selective for enkephalins.
- ○ Two subtypes (δ_1, δ_2) have been proposed:
  - – δ_1 receptors produce analgesia supraspinally.
  - – δ_2 receptors produce analgesia by spinal and supraspinal mechanisms.
- ○ Presently, there is no available therapeutic agent acting at δ receptors.

D. Sigma (σ) receptors

- ○ Are no longer considered to belong to the opioid class.
- ○ The receptor structure differs from opioids (e.g. no G protein coupling).

II. Physiological effects of opioids

- Analgesia (μ, δ, κ).
- Respiratory depression (μ_2 mainly).
- Gastrointestinal stasis (μ_2 mainly) is likely, especially with repeated use.
- Cardiovascular effects (mainly bradycardia).
- Histamine release leading to hypotension.
  - ○ More likely to occur with rapid IV administration.
- Central nervous effects (e.g. dysphoria, excitement)
  - ○ Can occur following opioid administration to unsedated horse.
  - ○ More likely to occur with IV administration (administer slowly).
  - ○ May be less likely to occur if horse is painful.
  - ○ Generally best to administer opioid IM in awake horse.
  - ○ Sedating the horse (e.g. α_2 agonist) prior to IV *morphine* is important.
- Hypothermia.
- Primarily metabolized in liver and excreted in urine.

III. Classification of commonly used opioids

A. Mu receptor agonists

- ○ Include *morphine*, *meperidine (pethidine)*, *fentanyl* and *methadone*.
  - – Analogs of fentanyl include *alfentanil*, *sufentanil* and *remifentanil*.
- ○ These agents are potent analgesics.

B. Mixed agonists/antagonists

- ○ Includes *butorphanol* and *pentazocine*.
- ○ Analgesic actions are mediated by κ_1 receptors.
- ○ *Butorphanol* and *pentazocine* have agonist activity at κ receptors and antagonist activity at μ receptors, and thus can be used to reverse the effects of μ agonists.
- ○ They may be described as having mixed agonist/antagonist activity at opioid receptors.

C. Partial agonists

- ○ *Buprenorphine* has partial agonist activity at μ receptors.
  - – It has high affinity at μ receptors but only limited activity.
- ○ It dissociates very slowly from μ receptors and is only weakly antagonized by *naloxone*.

D. Pure opioid antagonists

- ○ Include *naloxone*, *Nalmefene* and *naltrexone*.

IV. Clinical use of opioids

A. Sedation in association with α_2 agonists for standing restraint

- ○ Opioids potentiate the effects of α_2 agonists for standing sedation.
  - – *Morphine* (0.15 mg/kg, IV; 0.25 mg/kg, IM).
  - – *Butorphanol* (0.02–0.05 mg/kg, IV; 0.05–0.1 mg/kg, IM).
  - – *Meperidine* (*pethidine*) is administered IM (1–2 mg/kg).
    - ■ IV administration can result in histamine release and hypotension.
  - – *Methadone* (0.1 mg/kg) IV, IM.

B. Premedication prior to general anesthesia

- ○ May be especially helpful in calming a painful horse.
  - – For example, *morphine* (0.25 mg/kg) administration (IM, ~ 1 h prior to induction) with *acepromazine* (0.03–0.05 mg/kg).
  - – *Morphine* can be given alone (IM) if *acepromazine* is contraindicated.
- ○ *Butorphanol* (0.05–0.1 mg/kg, IM) is not as effective as *morphine*.
- ○ *Fentanyl* (1 µg/kg, IV) can be administered following α_2 sedation.
- ○ *Methadone* (0.1 mg/kg IV, IM). Use as for *morphine*.

C. Opioids in association with general anesthesia

o Opioids do not reduce volatile anesthetic MAC.
  – *Morphine* has been administered (0.15 mg/kg, IV) preoperatively (concurrent α_2 sedation followed by 0.1 mg/kg/h) or as an *intraoperative* bolus (0.1–0.17 mg/kg).
o *Morphine* may produce a more stable anesthesia.
  – Fewer supplemental doses of *ketamine* needed to prevent intraoperative movement.
  – The reported adverse effects of *morphine* do not differ from control horses.

D. Etorphine and acepromazine (Immobilon®) for neurolept anesthesia

o The combination of *etorphine* and *acepromazine* has been used for anesthesia of horses. The preparation is marketed with the opioid antagonist *diprenorphine*.
o Main advantages are its long duration of effect and reversibility.
o *Etorphine* is extremely potent and must be handled with great care.
  – It is rapidly lethal to humans. A reversal agent should be readily available in case of inadvertent injection or splashing of the drug into the eyes/mouth.
o Anesthesia of the horse with Immobilon® is characterized by:
  – Analgesia.
  – Anesthesia is relatively long-lasting.
  – Anesthesia is rapidly reversed by *diprenorphine*.
    ■ Re-sedation has been reported to occur following reversal.
    ■ This may reflect the shorter half-life of the antagonist.
  – Poor muscle relaxation (trembling of limbs is common).
  – Tachycardia.
  – Hypertension.
  – Hyperthermia.
  – Severe respiratory depression (cyanosis may be present).
  – The eyes remain open and should be protected.
  – Sweating.
  – Priapism is a common feature.

E. Opioids as analgesics

o Opioids can be used systemically as analgesics.
o IM administration is preferred as this will reduce the likelihood of excitement and may have a longer lasting effect.
o *Morphine* (0.25 mg/kg, IM). Analgesic effect lasts 4–6 hours.
o *Butorphanol* (0.05–0.1 mg/kg, IM). Short-lasting analgesia.
o *Methadone* (0.1 mg/kg, IM).
o Ileus is likely, especially with repeated use, so gastrointestinal motility should be closely monitored. Therefore, opioids should not be used long term to treat pain.

F. Epidural analgesia with opioids

o Opioids can be administered epidurally to produce analgesia in the awake horse or as adjuncts to general anesthesia. (See Chapter 17.)

o   *Morphine* (0.1 mg/kg) causes a modest decrease in *halothane* MAC.
–   Onset of analgesia is slow.
o   *Methadone* (0.1 mg/kg) produces analgesia of the perineum, and of the lumbar and caudal thoracic dermatomes.

G. Opioid antagonists

o   Are rarely indicated for reversal of opioid-induced effects.
o   *Diprenorphine* (marketed to reverse *etorphine*) is the exception.

Benzodiazepines

- Benzodiazepines are widely used in equine anesthesia, usually in combination with *ketamine* for induction of anesthesia.
- They are *not* used for standing sedation in the adult horse due to the muscle relaxation and ataxia which result.
- In neonatal foals, ataxia is less of a concern as the foal will become recumbent.
- There is the potential for mild excitement.

I. Benzodiazepines and receptor activity

- Benzodiazepines potentiate GABA responses at the $GABA_A$ receptor site by allosterically modulating GABA binding.
- This results in enhanced Cl^- influx at the $GABA_A$ receptor.

II. Physiological effects of benzodiazepines

- Muscle relaxation.
- Effects on cardiovascular function are minimal.
- Effects on respiration are minimal, when used alone.
  o   Combinations of benzodiazepines and *ketamine* should be given slowly to neonatal foals to avoid acute respiratory depression.

III. Benzodiazepines available for clinical use

- *Diazepam* and *midazolam* are most commonly used.

A. Diazepam

o   Not water-soluble (highly lipid-soluble).
o   Solvent (ethanol and propylene glycol) is irritating to tissues.
o   Emulsified solvent (less irritating) is available in some countries.
o   IM absorption is unpredictable.

- o   Has a long half-life.
- o   Metabolites are active.
  - –   Metabolized primarily in liver and excreted in urine.

B. Midazolam

- o   Water-soluble.
- o   Low lipid solubility at pH < 4; high lipid solubility at pH of plasma (7.4).
- o   No active metabolites.
- o   Non-irritating to tissues.
- o   Shorter half-life than diazepam.

C. Zolazepam

- o   Only available in combination with *tiletamine* (NMDA antagonist).
- o   Water-soluble.
- o   Species differences in metabolism rate for *zolazepam* and *tiletamine*.
- o   No information available on disposition kinetics in horses.

D. Climazolam

- o   Long half-life.
- o   There are few reports on its use in horses.
  - –   Has been used with *ketamine* for TIVA.
- o   Effects may have to be reversed after long procedures.

IV. Clinical use of benzodiazepines

A. Benzodiazepines for chemical restraint

- o   Not used for standing sedation in adults due to ataxia.
- o   Generally only used for sedation in *neonatal foals*.
  - –   Can be given alone or combined with low-dose *ketamine* for more profound sedation. Adding *ketamine* reduces the amount of benzodiazepine needed.

B. Induction of anesthesia

- o   In adult horses: *diazepam* or *midazolam* (0.02–0.05 mg/kg, IV) is commonly used with *ketamine* (2–2.5 mg/kg, IV) following α_2 sedation. This improves muscle relaxation and quality of induction.
- o   In neonatal foals: *diazepam* or *midazolam* (0.05–0.1 mg/kg, IV) can be used with *ketamine* (2–3 mg/kg) for induction without α_2 sedation.
- o   *Zolazepam* is used in combination with *tiletamine* for induction (1.0–1.5 mg/kg combined dose) following α_2 sedation.

C. Maintenance of anesthesia

- ○ *Midazolam* and *climazolam* have been used as part of TIVA.
  - – Reversal may be necessary after long-term administration (e.g. *climazolam*).
  - – Benzodiazepines may cause ataxia in recovery.
- ○ *Midazolam* has the shortest half-life and is more suited to TIVA.

D. Seizure control

- ○ Benzodiazepines can be used for the short-term control of seizures.

V. Antagonism of benzodiazepines

- *Flumazenil* (0.04 mg/kg, IV) is a specific antagonist and has been used for benzodiazepine reversal in foals.
- *Sarmazenil* (0.04 mg/kg, IV), which is not widely available, has been used to reverse *climazolam*.

Guaiphenesin

- *Guaiphenesin* is primarily used in equine anesthesia for its muscle-relaxing effects.
- It has minimal or no anesthetic properties and therefore should only be used to improve muscle relaxation in association with anesthetic drug regimens.

I. Mode of action of guaiphenesin

- *Guaiphenesin* is a centrally acting (brain stem and spinal cord) muscle relaxant, in contrast to drugs acting at the myoneural junction (e.g. *atracurium*).

II. Physiological effects

- Skeletal muscle relaxation, although high doses paradoxically cause muscle rigidity.
- Respiratory effects are minimal at recommended doses.
- Cardiovascular effects are minimal at recommended doses.
  - ○ May cause cardiovascular depression when combined with other anesthetic drugs.
- High concentrations (>10%) can cause hemolysis.
- Sedation is absent or minimal.
- Analgesia is *not* a feature.
- Metabolized by the liver and excreted in the urine.

III. Clinical use of guaiphenesin

- *Guaiphenesin should not generally be used to immobilize the awake horse*.
    - Its use may be indicated in certain emergency situations.
- It is inappropriate to use *guaiphenesin* in an attempt to deepen anesthesia.
- *Guaiphenesin* solutions can be irritating to tissues, and perivascular administration may cause a severe tissue slough. Therefore, use of a *jugular catheter* is advised.
- Since *guaiphenesin* is intended to be used *only* as a muscle relaxant, it is probably unnecessary to use concentrations > 5%, except in large horses.
    - Doses of 30–50 mg/kg are sufficient to produce relaxation in association with appropriate doses of sedative and anesthetics at induction.
    - Higher doses (50–100 mg/kg) are needed if lower doses of sedatives are used at induction.

A. To improve induction quality

- Following sedation (e.g. with *xylazine*, 0.3–1.0 mg/kg, IV) *guaiphenesin* can be administered alone until ataxia develops, at which time a bolus of *ketamine* (1.5–2.0 mg/kg, IV) or *thiopental* (3–5 mg/kg, IV) can be administered to cause unconsciousness.
- Alternately, *ketamine* or *thiopental* can be mixed with *guaiphenesin* and the combination infused to effect.

B. To maintain anesthesia with TIVA

- May be infused with anesthetic drugs (e.g. *xylazine*, *ketamine*) to improve muscle relaxation. (See Chapter 15.)
- May be infused with *thiopental* to maintain anesthesia for short periods (30–40 min).
- With long-duration infusions, *guaiphenesin* may contribute to ataxia in recovery. Use a low dose in such cases.

C. To maintain anesthesia with PIVA

- *Guaiphenesin* has been used with other drugs (e.g. *ketamine*) as part of PIVA (see Chapter 15), but it is probably unnecessary to use it for muscle relaxation as adequate relaxation will result from the administration of the inhalational anesthetic.

Tramadol

- *Tramadol* is classified as a centrally acting analgesic, with two distinct sites of action.
- It has not been investigated extensively in the horse.

I. Mode of action of tramadol

- Weak agonist activity at μ, κ and δ opioid receptors.
- Affinity at μ receptor is about 1/6000 that of *morphine*.

- Its active metabolite (M1) has a higher affinity (~ 200×) for μ receptor.
- *Tramadol*-induced analgesia is partially antagonized by *naloxone*.
  - This suggests non-opioid mechanisms of analgesia.
- Inhibition of re-uptake of norepinephrine and 5HT is considered to be the other mechanism of *tramadol*-induced analgesia.

II. Analgesic and antinociceptive effects

- Synergistic effect on descending inhibitory pathways in CNS.
- Modulation of second-order neurons in spinal cord.

III. Physiological effects

- *Comment*: limited information is available on the effects of *tramadol* in horses; most information comes from studies in human patients and laboratory animals.
- Analgesia.
  - Analgesic effects synergistic with NSAIDs.
  - Epidural administration (1 mg/kg) in the horse induces analgesia.
    - Equivalent to that produced by epidural *morphine* (0.1 mg/kg).
- Minimal effects on cardiorespiratory function.
- Sedation has been reported in the horse following *tramadol* (2.4 mg/kg, IV).
  - Sedation is equivalent to *xylazine* (0.3 mg/kg, IV).
- Effects on gastrointestinal motility are less than those of *morphine*.
- Organ toxicity is minimal.
- *Tramadol* is metabolized in the liver and forms a number of metabolites.
  - O-desmethyl (M1) metabolite is the only active metabolite *in vivo*.
  - Other metabolites do not cross blood–brain barrier.
- Excretion of *tramadol* and its metabolites is primarily via the kidneys.

IV. Clinical use of tramadol

  - Based on studies in other species and preliminary studies in horses, *tramadol* may have a role as an analgesic in horses.

Barbiturates

- *Thiopental* (*thiopentone*), a thiobarbiturate, is the only barbiturate in common use for anesthesia of the horse.
  - Thiobarbiturates have a sulphur moiety at C2 which increases potency and rapidity of effect, and shortens the duration of action.
- *Pentobarbital* (*pentobarbitone*) has been used for producing anesthesia of longer duration, but prolonged administration or a high dose causes a poor recovery.

I. Receptor activity of barbiturates

- Barbiturates directly activate the $GABA_A$ receptor, thereby mediating Cl^- influx.

II. Physiological effects of thiopental

- Depend on the dose used and whether other drugs are administered concurrently.
- Cardiovascular effects are more pronounced in states of cardiovascular compromise.
- Hypotension results from venodilation and the resulting decrease in preload.
- Myocardial depression is insignificant with low doses, but significant with high doses.
- Myocardium becomes more sensitive to catecholamines.
- Respiratory depression can be significant with high doses.
- Analgesia is *not* a feature of barbiturate anesthesia.

III. Pharmacokinetic properties of thiopental

- The short duration of action following a bolus is due to redistribution.
- Initial redistribution is to muscle.
- Clearance is low.
- Prolonged recovery following infusions is related to the long terminal half-life.
- The long *context-sensitive* half-life makes it unsuitable for prolonged infusion.
- Ultimate elimination is via hepatic extraction.
- No active metabolites.

IV. Clinical use of thiopental

- *Thiopental* is infrequently used nowadays for induction and has been replaced to a large extent by *ketamine*.

A. Induction of anesthesia following minimal or no sedation

- ○ It is possible to induce anesthesia with *thiopental* in unsedated or minimally sedated (e.g. *acepromazine*) horses, but this technique is *not recommended*.
  - – Large doses of *thiopental* (~10 mg/kg) are required, necessitating a concentrated solution which is irritating to tissues.
- ○ Induction is uncontrolled and recovery is generally not smooth.
- ○ Experienced personnel are needed to facilitate induction.
- ○ Cardiorespiratory depression occurs.
- ○ No analgesia results.

B. Induction of anesthesia following alpha$_2$ agonist

- ○ *Thiopental* can be used satisfactorily to induce anesthesia following sedation with an α_2 agonist.
  - – A lower dose of *thiopental* can be used (3–5 mg/kg, IV).

- o Less cardiorespiratory depression.
- o Induction and recovery are improved.
- o Analgesia is improved.
- o Induction onset is slow.
  - – Due to prolonged circulation time from α_2 effects.

C. Induction of anesthesia with guaiphenesin

- o *Thiopental* can be combined with *guaiphenesin* and given as an infusion.
  - – A lower dose of *thiopental* (3–4 mg/kg) can be used.
- o This method will induce recumbency and/or unconsciousness (depending on the dose of *thiopental*) without premedication, but sedation is recommended.
- o Induction is smooth, especially if the horse is sedated.
- o The mixture alone has no analgesia.
- o Large doses of *guaiphenesin* may contribute to weakness in recovery.

D. Maintenance of anesthesia with guaiphenesin

- o *Thiopental* can be infused with *guaiphenesin* to maintain anesthesia.
  - – For adult horse (400–500 kg), *thiopental* (2–3 g) is added to 1 liter of 5% *guaiphenesin* and infused at 2–3 ml/kg/h.
- o Prolongs anesthesia (α_2/*ketamine* induction) by 30–40 minutes.
- o To prevent excessive administration of *thiopental*, use a different agent for induction.
  - – Can be used following α_2/*ketamine* induction.

V. Clinical use of pentobarbital

A. Use following acepromazine

- o *Pentobarbital sodium* has been used in equine anesthesia, and a favorable report of its use in clinical cases following *acepromazine* tranquilization is reported.
- o A total of 20 mg/kg IV is given initially.
  - – Half of the initial dose is injected rapidly.
  - – The remainder is given at a slow rate until the horse falls (~30 seconds).
- o Smaller 'top up' doses (2 mg/kg) can be given to increase anesthetic depth.
- o The duration of surgical anesthesia with this regimen is about 20 minutes.
- o Recovery is gradual and controlled and is completed in 20–45 minutes.

B. Use following alpha$_2$ agonists

- o *Pentobarbital* use in research ponies indicated that, following *xylazine* (1.1 mg/kg, IV) sedation, *pentobarbital* (~12 mg/kg, IV) is acceptable for induction.

C. Use for euthanasia

- o Concentrated solutions of *pentobarbital* are used for euthanasia. (See Chapter 23.)

Ketamine

- Widely used as an induction agent for horses.
- Can be used, at sub-anesthetic doses, for analgesia in awake horses.
- Available commercially as a racemic mixture of the $(S)^{(+)}$ and $(R)^{(-)}$ enantiomers.
  - The $(S)^{(+)}$ is more potent in terms of anesthesia.

I. Ketamine and receptor activity

- Effects are *not* linked to $GABA_A$ receptor mechanisms, thus making it distinctive among anesthetics.
- Produces its anesthetic effects by inhibiting excitatory synaptic transmission which is mediated by noncompetitive antagonism of the N-methyl-D-aspartate (NMDA) receptor.
- Has effects at other receptors (opioid, muscarinic, nicotinic) but these do not appear to be significant as regards its anesthetic action.
  - Analgesic effects of *ketamine* are *not* reversed by *naloxone*.

II. Unique anesthetic effects of ketamine

- *Ketamine* produces a state of *dissociative anesthesia*.
  - This state is based on EEG findings of a dissociation of the thalamocortical (synchronous δ waves are present) and limbic (θ waves are evident) systems. It is characterized by:
    - Analgesia.
    - Amnesia.
    - Catalepsy.
      - Catalepsy is an akinetic state with loss of orthostatic reflexes in which the patient appears paralyzed by motor and sensory failure.

III. Physiological effects of ketamine

- Many of the reported cardiovascular effects attributed to *ketamine* are based on its use without prior sedation, and they may not apply to situations where it is used in association with sedatives.
- Analgesia.
  - Inhibition of excitatory glutaminergic transmission (NMDA receptor) at spinal and supraspinal sites.
- MAC reduction.
- Direct myocardial depression, but this is masked by the sympathetic stimulation which occurs in most cases.
  - Results in increased cardiac output, blood pressure, and heart rate.
- Respiratory depression is minimal.
- Bronchodilation.
- Minimal effect on gastrointestinal motility.
- *Ketamine* is metabolized in the liver and excreted by the kidneys.

IV. Clinical use of ketamine

A. Induction of anesthesia following alpha$_2$ agonist sedation

- In adult horses, *ketamine* (2–2.5 mg/kg, IV) may be used alone, or with a benzodiazepine, for induction following α_2 agonist sedation.
- In neonatal foals, *ketamine* (2–3 mg/kg, IV) can be used with a benzodiazepine for induction without prior sedation.
- The duration of surgical anesthesia is short (5–10 minutes).
- Anesthesia may be prolonged by using intermittent boluses of *ketamine* and the α_2 agonist.
  - One-quarter to one-half of the initial dose of the α_2 agonist and *ketamine* can be administered as needed.
  - Re-dosing the benzodiazepine may produce ataxia in recovery.

B. To maintain anesthesia

- *Ketamine* may be used as a component of TIVA or PIVA. (See Chapter 15.)

C. Epidural ketamine

- The MAC reduction is modest with epidural *ketamine*.
- Duration of action appears to be short and dose-dependent.

D. Analgesia in the awake horse

- There are limited data on these methods.
- *Ketamine*, alone, can be safely infused at up to 0.4–0.8 mg/kg/h.
- *Ketamine* (0.2 mg/kg/h) can be combined with *lidocaine* (3 mg/kg/h).
  - The loading dose of both drugs [*ketamine* (1 mg/kg, IV) and *lidocaine* (2.0–2.5 mg/kg, IV)] can be combined and infused over 30 minutes.

E. Low-dose ketamine with α_2 agonist for standing sedation or analgesia

- *Ketamine* (0.1–0.2 mg/kg, IV) can be given with a low dose of α_2 agonist (e.g. *xylazine* 0.3 mg/kg, IV) to intensify the analgesia from the α_2 agonist.
- Ataxia will develop if high doses of an α_2 agonist are used concurrently.

Tiletamine and zolazepam (TZ)

- *Tiletamine* and *zolazepam* are commercially (Telazol®, Zoletil®) available as a 1:1 combination of 250 mg of each drug in powder form.
- This combination can be used as an induction agent in equine anesthesia following sedation with an α_2 agonist.

I. Receptor activity of TZ

- *Tiletamine*, like *ketamine*, produces its anesthetic effects by inhibiting excitatory synaptic transmission which is mediated by noncompetitive antagonism of the N-methyl-D-aspartate (NMDA) receptor.
- *Zolazepam* is a benzodiazepine and thus potentiates GABA responses at the $GABA_A$ receptor site by allosterically modulating GABA binding.

II. Physiological effects

- The effects of *tiletamine* are basically similar to those of *ketamine*.
- *Zolazepam* is a long-acting benzodiazepine.

III. Clinical use of TZ

- When used alone, *TZ* is a poor analgesic.
- Not recommended for anesthesia induction in the unsedated horse.
- Combining with α_2 agonist improves analgesia and induction.

Induction of anesthesia following α_2 agonist sedation
  - *TZ* (1–2 mg/kg, IV) can be used to induce anesthesia following α_2 sedation.
  - *TZ* (1.5 mg/kg, IV) has a duration of surgical anesthesia twice that of *ketamine* (2.2 mg/kg).
  - Inductions are excellent following α_2 sedation.
  - Recoveries are acceptable – but not quite as good as α_2/*ketamine*.
  - Recoveries may be better if longer-acting α_2 agonists used.
  - Recoveries are better with *lower* doses (1.0–1.25 mg/kg) of *TZ*.
  - For *large horses*, *TZ* may be reconstituted with *ketamine*.
    - *Example*: For a 600 kg horse, add 500 mg *ketamine* to 500 mg *TZ* (0.83 mg/kg).

Propofol

Propofol is not in common use in equine anesthesia partly because of cost, but also because of the large volume needed for induction and the often poor quality of induction.

I. Propofol and receptor activity

- Potentiates and has a direct gating effect on $GABA_A$ receptors at spinal and supraspinal synapses, thereby facilitating inhibitory synaptic transmission.
- Blocks Na^+ and Cl^- channels.
- Can potentiate glycine receptors.

II. Physiological effects of propofol

- Hypotension (due to a decrease in systemic vascular resistance and venous return).
- Little direct myocardial depression.
- Respiratory depression is marked and is dose-dependent.
- Analgesia is minimal.
- Synergistic with many other anesthestic agents.
  - Thus allowing a lower dose of *propofol* to be used.
- Minimal organ toxicity.
- Primarily metabolized by the liver, and inactive metabolites are excreted in the urine.
  - Clearance exceeds hepatic blood flow suggesting that extrahepatic metabolism occurs.

III. Unique features of propofol

- *Propofol* is a lipophilic phenol which is formulated as an oil/water emulsion containing soya bean, egg lecithin, and glycerol.
- The emulsion serves as a good medium for microbial growth, and since no antimicrobial compound is added contamination can occur once the vial is opened.
  - Unused *propofol* should be discarded after 6 hours.

IV. Clinical use of propofol

- *Propofol* does not seem to be suitable for induction of anesthesia in the *unsedated* horse.
- Combining *propofol* with α_2 agonists improves the quality of induction.
- Myoclonus and paddling with the limbs have been reported, even with sedation.

A. Induction of anesthesia following α_2 agonist sedation

- Following routine α_2 agonist sedation (e.g. *xylazine* 1.1 mg/kg, IV), 2 mg/kg of *propofol* seems to be the most appropriate dose.
  - However, some horses show excitement even with α_2 sedation.
- *Midazolam* (0.02 mg/kg, IV) does not seem to improve induction.
- *Propofol* has no advantage over *ketamine* induction and, in general, the quality of inductions is poorer than with *ketamine*/α_2 agonist.
- Foals require slightly higher induction and maintenance doses than do adults, because they have a proportionally larger central compartment.

B. To maintain anesthesia (see TIVA and PIVA–Chapter 15.)

- *Propofol* is considered a close to ideal agent for infusions due to:
  - Short, context-sensitive half-life.
  - Rapid clearance.
- *Propofol* can be used as the sole agent for TIVA or as a component of TIVA or PIVA.

	Inhalational anesthetics

- Inhalational anesthetics, with the exception of N_2O, are widely used to maintain anesthesia in horses.
- Newer anesthetics are less lipid soluble (lower blood/gas partition coefficient), less potent (higher minimum alveolar concentration) and less cardiovascular depressive.
- Inhalational anesthetics are *not* good analgesics.
- Inhalational anesthetics can be combined with injectable anesthetics to produce balanced anesthesia. (See PIVA–Chapter 15.)

I. Mode of action

- Inhalational anesthetics enhance actions of a number of receptors, including $GABA_A$ and glycine.
- They inhibit nicotinic, acetylcholine, serotonin, and glutamate receptors.
- $GABA_A$ receptors are the most abundant inhibitory neurotransmitter receptors in the brain and have received the most attention regarding the mode of action of inhalational anesthetics.

II. Pharmacokinetics

- The uptake and the distribution of inhalational anesthetics are determined by physico-chemical properties of the drug. (See Table 11.1.)
- The increase in the anesthetic concentration in the alveoli (*wash-in*) and subsequent uptake by the blood (*distribution*) is determined primarily by factors which affect:
  - The rate of delivery to the alveoli.
  - The rate of removal from the alveoli.

Table 11.1   Physicochemical properties of common inhalational anesthetics.

	Halothane	Isoflurane	Sevoflurane	Desflurane	N_2O
MAC (%)	0.82–0.95	1.31	2.31	7.6	205
Blood/gas partition coefficient	1.66	0.92	0.47	0.42*	0.47*
*Brain/blood partition coefficient	2.9	2.6	1.7	1.3	1.1
Vapor pressure (mmHg at 20°C)	243	238	157	660	–
Molecular weight (D)	197	185	200	168	44
Biotransformation (%)	20	0.2	5	0.02	0.004
Chemical classification	Halogenated alkane	Halogenated ether	Halogenated ether	Halogenated ether	Other

* Human data.

III. Rate of delivery of anesthetic to the alveoli

- Is affected by the inspired concentration of anesthetic and alveolar ventilation.

A. Inspired concentration

- ○ The higher the vaporizer dial setting, the faster the pressure gradients are established and equilibrium achieved.
- ○ Inspired concentrations several times in excess of minimum alveolar concentrations are necessary (due to the horse's size) initially to overcome the effects of dilution in the anesthetic equipment and the time taken to saturate tissues.
- ○ Use of high oxygen flows (10–20 ml/kg/min) in the first 10 to 15 minutes overcomes the dilution effect of the anesthetic equipment and facilitates the increase in the alveolar concentration of the inhalational anesthetic.
  - – Large animal anesthetic machines have an internal volume of 30–50 liters.

B. Alveolar ventilation

- ○ The more efficient breathing is, the better the delivery of inhalational anesthetics to the alveoli for uptake and distribution.
- ○ Tidal volume and respiratory rate need to be sufficient to assure adequate uptake.
  - – Positive pressure ventilation assures more effective delivery of anesthetic.

IV. Rate of removal of anesthetic from the alveoli

- Is dependent on a number of factors including drug solubility and cardiac output.
- The axiom is that once a constant alveolar concentration is achieved, a similar concentration is reached in the brain.
- *Delivered concentration > Inspired > Alveolar > Blood > Brain concentration.*
  - ○ The reverse process occurs in recovery after discontinuing delivery.

A. Solubility of the anesthetic

- ○ Lipid solubility is expressed as the partition coefficient of blood/gas, which determines the uptake of anesthetic from the alveoli into the blood after an equilibration period between the two phases.
  - – Drugs with blood/gas partition coefficients < 1 are considered to have low lipid solubility (e.g. *desflurane*). For *desflurane*, at equilibrium there is less than half the concentration of anesthetic in blood than in the alveoli.
  - – Drugs with higher lipid solubility (e.g. *halothane*) take longer to achieve the desired concentration in the alveoli and the brain, since more drug is distributed through the blood into tissues.
- ○ Lipid solubility determines the onset time of anesthetic effect and duration of action.
- ○ Induction and recovery, as well as changes in anesthetic depth, will require a longer period for halothane than for anesthetics (e.g. *desflurane*) with low lipid solubility.

B. Cardiac output

○ The higher the blood flow to the lungs, the greater the uptake of drug from the alveoli. This reduces the alveolar concentration and therefore brain concentration.
○ Animals with impaired cardiovascular function achieve alveolar concentrations and therefore brain concentrations *faster* than healthy animals.
  – Therefore, great care must be taken when inducing such horses (see foal anesthesia, Chapter 15) with an inhalational anesthetic.

C. Tissue capacity and blood flow to the tissue

○ Drugs with higher lipid solubility tend to saturate other tissues besides the brain, therefore the distribution of the inhalational anesthetic takes longer.
○ Consequently, induction and recovery are prolonged.

V. Minimum alveolar concentration (MAC)

● MAC is the minimum alveolar concentration necessary to prevent purposeful movement in response to a noxious stimulus (e.g. tail clamp or electrical stimulation of the skin of the extremities, oral mucosa, or hoof area) in 50% of test subjects.
  ○ MAC is a measure of *potency* and allows comparison among anesthetics.
  ○ Drugs with a lower MAC are more potent than drugs with a higher MAC.
  ○ The higher the solubility (blood/gas or oil/gas partition coefficient) the lower the MAC.

A. MAC and surgical anesthesia

○ To prevent movement during surgical procedures it is generally necessary to maintain end-tidal concentrations about 30% greater than the MAC.
○ For non-painful procedures (e.g. radiography) end-tidal concentrations can approximate MAC.
○ Sedative/analgesic drugs generally allow lower end-tidal concentrations to be used.

B. Factors which decrease MAC

○ Hypothermia.
○ Extremes of age.
  – MAC is lower in neonates and older individuals.
○ Sedatives and analgesics (opioids are an exception in the horse).
○ Pregnancy.
○ Endotoxemia.

C. Factors which increase MAC

○ CNS stimulants (e.g. amphetamines).
○ Age.
  – MAC increases until adulthood then decreases.
○ Hyperthermia.

D. Drugs shown to decrease MAC in horses

○ *Acepromazine* (0.05 mg/kg IV, ↓ *halothane* MAC ~ 30%).
○ Alpha$_2$ agonists (dose-dependent decrease).
  – *Xylazine* (0.5 mg/kg IV – ↓ *isoflurane* MAC ~ 25%; 1 mg/kg IV – ↓ *isoflurane* MAC ~ 35%). Effect decreases over time.
  – *Detomidine* (30–60 µg/kg IV – ↓ *isoflurane* MAC ~ 35–45% for 90 minutes).
  – *Medetomidine* (3.5 µg/kg/h IV – ↓ *desflurane* MAC ~ 30%).
○ *Ketamine* (dose-dependent, 30–50 µg/kg/min – ↓ *halothane* MAC 25–35%).
○ Opioids have a variable effect, but generally do not decrease MAC.
  – CNS excitation predominates over their analgesic effect.
○ Benzodiazepines:
  – *Diazepam* (0.05 mg/kg IV – ↓ *halothane* MAC ~ 30%).
○ *Lidocaine* (dose-dependent effect)
  – At 50–100 µg/kg/min – ↓ *halothane* & *isoflurane* MAC 25–50%.
○ N$_2$O (dose-dependent effect)
  – A 25–50% inspired concentration – ↓ *halothane* MAC 12–25%.

VI. Physiological effects

A. Cardiovascular effects

○ Dose-dependent cardiovascular depression.
  – *Isoflurane*, *sevoflurane*, and *desflurane* induce less depression than *halothane*.
○ Cardiac output decreases due to decreased contractility.
○ Hypotension secondary to a decrease in vascular resistance and contractility.
○ Stroke volume is reduced due to decreased contractility.
○ Heart rate decreases or remains unchanged.
○ Inhalational anesthetics sensitize the myocardium to catecholamines, resulting in dysrhythmias.
  – Alkanes (*halothane*) are more arrhythmogenic than ethers (e.g. *isoflurane*).

B. Respiratory effects

○ Dose-dependent respiratory depression.
○ Inhalational anesthetics decrease respiratory rate resulting in increased PaCO$_2$.
  – *Halothane* decreases respiratory rate less than modern drugs.
  – *Halothane* decreases tidal volume more than modern drugs.
○ Minute ventilation is similar among inhalational anesthetics, resulting in comparable PaCO$_2$.

C. Renal effects

○ Decreased blood flow.
○ Decreased glomerular filtration.
○ Decreased urine output.

D. Hepatic effects

- ○ Decreased hepatic blood flow.
  - – *Halothane* decreases blood flow more than modern inhalational drugs.
  - – *Halothane* depresses hepatic function more than modern inhalational drugs.
- ○ *Halothane* may cause a transient increase in liver enzyme activity.

E. Muscle relaxation

- ○ Excellent muscle relaxation.
- ○ Potentiate muscle-relaxing drugs.

F. Analgesia

- ○ Poor analgesics.
  - – Supplemental analgesics are recommended during surgical procedures.

Nitrous oxide

- The MAC for *nitrous oxide* (N_2O) is over 200%, indicating that it cannot be used as the sole anesthetic in horses.
- However, it can be used as an adjunct to other anesthetics.
- MAC reductions of 12–25% are achieved with 25–50% inspired concentrations.
- Clinically, in other species, N_2O is administered in concentrations of 60–70% with oxygen (30–40%); however, these low inspired oxygen fractions increase the likelihood of hypoxemia in the horse.

I. Mode of action

- N_2O exhibits inhibitory actions on neuronal nicotinic ACh receptors and N-methyl-D-aspartate.
- N_2O differs from volatile anesthetics in that it has no effects on $GABA_A$ and glycine receptors.

II. Pharmacokinetics

- N_2O's low lipid solubility (blood/gas partition coefficient of 0.47) allows rapid achievement of alveolar and brain partial pressure during induction and also rapid removal during recovery.
- Administration of high concentrations of N_2O accelerates the rate of rise in the alveolar concentration of other inhalational anesthetics (second gas effect).
  - ○ Effect is unlikely to be clinically significant in the horse.
- Biotransformation is minimal (0.004%).

III. Potential advantages of N$_2$O

- Rapid achievement of alveolar concentrations.
- Analgesia.
- Less cardiorespiratory depression than other inhalational anesthetics.
- MAC reduction of other inhalational anesthetics.

IV. Potential disadvantages of N$_2$O

- Risk of hypoxemia due to:
  - Lowered FIO$_2$.
    - Due to the relatively high inspired fraction of N_2O.
  - Inappropriate flows of either N_2O or O$_2$.
  - Leaks in the circuit causing a reduction in inspired O$_2$.
- Absorption into air-containing cavities (e.g. gastrointestinal tract).
  - N_2O displaces nitrogen, and this may result in distension of the cavity.
  - N_2O is 30 times more soluble than nitrogen.
- Diffusion hypoxia during recovery is a risk if O$_2$ administration is not continued for a period of time after N_2O administration ceases.
- Pollution.
  - Risk of megaloblastic anemia subsequent to inactivation of methionine synthetase.
  - N_2O has an extremely long half-life in the atmosphere.

V. Clinical use of N$_2$O

- Due to the disadvantages and relative impotency of N_2O, it is difficult to justify its clinical use in the horse.

Local anesthetics

Leigh Lamont

Local anesthetics reversibly block the generation and propagation of electrical impulses in a variety of excitable tissues. Common therapeutic targets include peripheral nerves, spinal nerve roots, and the spinal cord. Skeletal muscle, cardiac muscle, and the brain are also affected.

I. Peripheral nerve fiber anatomy

- Peripheral nerves are mixed, contain afferent and efferent fibers, and may be myelinated or unmyelinated.
- Nerve fibers are commonly classified by size, conduction velocity, and function. (See Table 11.2.)

Table 11.2 Classification of nerve fibers.

Classification	Function	Diameter (μm)	Myelination	Conduction velocity (m/s)	Sensitivity to blockade
Type A					
alpha	Proprioception, motor	12–20	Heavy	70–120	+
beta	Touch, pressure	5–12	Heavy	30–70	++
gamma	Muscle tone	3–6	Heavy	15–30	++
delta	Pain, temperature	2–5	Heavy	12–30	+++
Type B	Preganglionic autonomic	< 3	Light	3–15	++++
Type C					
dorsal root	Pain	0.4–1.2	None	0.5–2.3	++++
sympathetic	Postganglionic	0.3–1.3	None	0.7–2.3	++++

- Individual nerve fibers (axons) travel together as fascicles within an outer sheath (perineurium).
- Myelinated nerve fibers are segmentally enclosed by Schwann cells forming multiple layers of myelin. Periodic interruptions in the myelin sheath are called nodes of Ranvier where structural elements for neuronal excitation are concentrated.
- Multiple unmyelinated nerve fibers are surrounded by a single Schwann cell membrane.

II. Electrophysiology of neural conduction

- Electrically excitable membranes associated with nerve axons and neuronal bodies maintain a transmembrane potential of −90 to −40 mV.
- During excitation, membrane Na^+ channels are activated (open) and Na^+ ions flow into the cell, rapidly depolarizing the membrane. After depolarization, Na^+ channels are inactivated (closed) and K^+ channels open. The outward flow of K^+ repolarizes the membrane and returns the Na^+ channels to the resting (closed) state.
- An action potential (AP) is generated by membrane depolarization when the impulse firing threshold is reached.
- After generation of the AP, propagation is required for transmission along the nerve fiber.
- Impulse generation and propagation are 'all or none' phenomena.
- Nonmyelinated fibers require threshold potential to be reached at the immediately adjacent section of membrane. Myelinated fibers require threshold to be reached at the next node of Ranvier (saltatory conduction), facilitating more rapid neural transmission in these fibers.

III. Mechanism of action of local anesthetics

- At the level of a single ion channel, a local anesthetic molecule binds to a specific receptor located on the intracellular side of a voltage-gated Na^+ channel and inhibits Na^+ inflow.
- At the level of the nerve fiber, as more and more Na^+ channels are bound by local anesthetic molecules, the threshold for excitation increases, impulse conduction slows, the rate of rise of the AP declines, the AP amplitude decreases, and finally generation of the AP fails.

- Increasing the frequency of nerve membrane depolarization increases the probability that Na^+ channels will exist in the open and inactive forms (vs. the resting form) which exhibit greater affinity for local anesthetic molecules. Thus, a stimulated nerve is more susceptible to conduction blockade than a nonstimulated nerve. This is called *use-dependent block*.
- Certain fibers within a single peripheral nerve are blocked before others. Sympathetic function tends to be blocked first, followed by pain sensation, touch and temperature discrimination, and finally motor function. (See Table 11.2.) This is called *differential block*, and the exact mechanism of this phenomenon has not been conclusively proven.
- In addition to their effects at Na^+ channels, local anesthetics delivered into the subarachnoid or epidural space may contribute to antinociception by modulating levels of various neurotransmitters including substance P, ACh, and GABA in the spinal cord dorsal horn.

IV. Physicochemical properties of local anesthetics

A. Physical properties

- The local anesthetic molecule has three components:
  - A *lipophilic group* (usually an aromatic ring).
  - A *hydrophilic group* (usually a tertiary amine).
  - A *connecting intermediate chain* (including either an ester or an amide linkage).
- Local anesthetics are classified based on the connecting intermediate chain and are referred to as either *aminoesters* or *aminoamides*.

B. Factors affecting activity and potency

Hydrogen ion concentration
- Local anesthetics are weak bases which are available commercially as salts.
- In aqueous solutions, these salts dissociate into non-ionized (neutral, lipophilic) and ionized (charged, hydrophilic) forms depending on the pH of the environment and the pK_a (dissociation constant) of the drug. (See Table 11.3.)
- Non-ionized and ionized forms of the molecule may be involved in Na^+ channel blockade.
- While non-ionized molecules appear to be less active at the Na^+ channel receptor, this form can rapidly gain access to the intracellular channel binding site by diffusion.
- Ionized molecules exert greater activity at the Na^+ channel receptor but can only access the intracellular channel binding site by passing through the hydrophilic Na^+ channel pore.
- Local anesthetics with a lower pK_a have a greater percentage of drug available as the non-ionized form, and so more drug is able to diffuse across the axonal membrane. Once inside the cell, the non-ionized drug is rapidly protonated and is able to maximally activate the Na^+ channel receptor binding site and produce a clinical effect.

Lipid solubility
- Increased drug lipid solubility tends to slow the rate of onset of action, increase the duration of action, and increase potency.

Table 11.3   Physicochemical properties of selected local anesthetics.

Local anesthetic	pK_a	% Ionized at pH 7.4	Partition coefficient (lipid solubility)	% Protein binding
Aminoesters				
Procaine	8.9	97	100	6
Aminoamides				
Lidocaine	7.9	76	366	64
Mepivacaine	7.6	61	130	77
Bupivacaine	8.1	83	3420	95
Ropivacaine	8.1	83	775	94

Protein binding
- o   Increased plasma protein binding tends to be associated with increased duration of action.

Stereoisomerism
- o   Most local anesthetics are asymmetrical molecules that exhibit two distinct spatial arrangements (mirror images), despite having the same physicochemical characteristics.
- o   Stereoisomers may possess differing potencies, pharmacokinetic properties, and toxicities.

V. Pharmacokinetics of local anesthetics

A. Absorption

- o   Systemic absorption of a local anesthetic is dependent on a number of factors:

Dose
- o   The greater the dose injected, the greater the systemic absorption and peak blood concentration (C_{max}).

Injection site
- o   Administration into a highly vascular area (e.g. mucosal, pleural or peritoneal surfaces) results in rapid absorption and higher blood concentrations compared with injection into less perfused areas (e.g. subcutaneous tissue, perineural fat).

Drug–tissue binding
- o   The more potent local anesthetics with greater lipid solubility and protein binding are associated with lower systemic absorption and C_{max}.

Vasoconstrictors
- o   The addition of *epinephrine* will counteract the inherent vasodilating properties of most local anesthetics.
  - –   The reduction in C_{max} with *epinephrine* is most significant with the less lipid soluble, less potent, shorter-acting agents (e.g. *lidocaine*).

    o   With more potent, longer-acting agents (e.g. *bupivacaine*), the impact of local blood flow on systemic absorption tends to be less significant.

B. Distribution

    o   Due to their rapid metabolism and short plasma half-lives, distribution of ester-type agents is limited.

    o   Conversely, amide local anesthetics are widely distributed after intravenous administration according to a two- or three-compartment model.

Effect of pulmonary uptake

    o   Local anesthetic that is absorbed into the venous circulation is initially distributed to the lungs where substantial uptake occurs.

    o   This limits the amount of drug reaching the systemic circulation and the vessel-rich tissues and may limit toxicity.

Effect of hypercapnia

    o   Development of hypercapnia for any reason will increase regional cerebral blood flow and may result in increased concentrations of local anesthetic being delivered to the brain, which may increase the risk of toxicity.

C. Metabolism and excretion

    o   Biotransformation of local anesthetics depends on the chemical structure of the drug.

Aminoester metabolism

    o   These agents are rapidly hydrolyzed in the blood (and to a lesser extent in the liver) by non-specific pseudocholinesterases.

    o   The rate of hydrolysis varies (*chloroprocaine > procaine > tetracaine*), but clearance is generally rapid and half-lives are measured in minutes.

    o   *Para-aminobenzoic acid (PABA)* is a breakdown product of ester metabolism.
        – Responsible for rare allergic reactions.

Aminoamide metabolism

    o   These agents are hydrolyzed by the liver cytochrome P450 enzyme system.

    o   The rate of hepatic metabolism varies (*etidocaine > lidocaine > mepivacaine > ropivacaine > bupivacaine*), but clearance is slower than that of the esters, and half-lives are measured in hours.
        – Reduced hepatic biotransformation and clearance of amide local anesthetics may prolong duration of action and increase the risk of toxicity.
        – Decreased hepatic function and/or blood flow, and concurrent administration of drugs which undergo metabolism through the P450 enzyme system, may affect hepatic metabolizing capability.
        – *Ortho-toluidine* is a breakdown product of amide metabolism, most notably of *prilocaine*, that is capable of oxidizing hemoglobin and may cause methemoglobinemia.

VI. Local anesthetic adjuvants and combinations

A. Epinephrine

- o 5 µg/ml may be added to a local anesthetic solution to decrease local perfusion, delay absorption, and prolong anesthetic action.
- o When administered into the epidural or subarachnoid spaces, *epinephrine* may enhance analgesia through interaction with α-adrenergic receptors in the spinal cord and brain.

B. Alpha$_2$ agonists

Effects on peripheral nerve blocks
- o Studies suggest that the addition of an α$_2$ agonist may potentiate peripheral nerve blocks with local anesthetics in human patients.
  - – Whether this interaction is pharmacodynamic, pharmacokinetic, or a combination of the two is unclear.
  - – This effect has *not* been documented in the horse.

Effects on epidural anesthesia
- o Adding *xylazine* to *lidocaine* potentiates and prolongs anesthesia when administered into the caudal epidural space in horses.
  - – This synergism is presumably due to activation of α$_2$ adrenergic receptors in the spinal cord dorsal horn which inhibits release of substance P and hyperpolarizes nociceptive projection neurons.
  - – This combination is used commonly in clinical equine practice for caudal epidural anesthesia.

C. Bicarbonate

- o 1 mEq/10 ml added to a local anesthetic solution to increase the pH increases the amount of non-ionized drug available to diffuse across membranes and accelerates the action.
  - – The clinical benefits of this practice remain debatable.

D. Hyaluronidase

- o This enzyme may be added to a local anesthetic solution to break down hyaluronic acid which functions as mesenchymal tissue cement.
  - – In theory, this may improve diffusion of the local anesthetic.

E. Carbon dioxide

- o Carbonation of local anesthetic solutions causes local intracellular acidosis which, in theory, increases the amount of intracellular ionized drug available to bind Na^+ channel receptors and accelerates the onset of action.
- o This practice does not appear to significantly improve block quality in *equine* patients.

F. Combinations of local anesthetics

○ The combination of a quick-onset, short-acting, local anesthetic with a slow-onset, long-acting, local anesthetic has theoretical merit.

○ There is currently no evidence to suggest that this practice is clinically beneficial.

VII. Local anesthetic toxicity

● When used correctly, local anesthetics have proven to be safe, and adverse effects are not common.

● Toxicities can be divided into three categories: systemic, local tissue toxicity, and allergic.

A. Systemic toxicity

○ This is most often the result of inadvertent and rapid intravenous infusions producing a dose-dependent continuum of effects on the brain and heart.

Central nervous system

○ In most species, the relative CNS toxicity of various local anesthetics is proportional to their potencies.

○ In horses, *procaine* is an exception to this rule, demonstrating a low anesthetic potency but a high propensity to cause CNS stimulation in this species (see below).

○ Low doses of local anesthetics tend to produce CNS depression, while higher doses cause CNS excitation.

○ Significant CNS excitation is evident after IV boluses of approximately 2.5 mg/kg of *procaine* in horses and is characterized by deep, rapid and forced inhalations, fine muscle tremors, pawing at the ground, and excessive pacing.

○ Skeletal muscle tremors are usually the first *signs of toxicity* in horses, and progress to seizures, unconsciousness, coma, and respiratory arrest.

– Muscle tremors are evident at serum *lidocaine* concentrations of approximately 3 µg/ml in horses, or with IV boluses of approximately 4–6 mg/kg.

– Seizures are induced with IV boluses of approximately 6–8 mg/kg.

– Adult horses safely tolerate up to 250 ml of 2% *lidocaine* (~ 11 mg/kg) for infiltration of the paralumbar fossa for abdominal surgery.

– Benzodiazepines, barbiturates, inhalational anesthetics, and potentially propofol are effective in treating local anesthetic induced seizures.

○ Seizure activity is exacerbated by hypercapnia and acidosis, thus moderate hyperventilation and oxygen supplementation are indicated in cases of toxicity.

Cardiovascular system (CVS)

○ Significantly higher serum concentrations of local anesthetic are required to produce CVS toxicity compared with CNS toxicity.

○ Characteristics of CVS toxicity vary with the local anesthetic involved.

– All may decrease myocardial contractility.

– The less potent agents (*lidocaine*, *mepivacaine*) cause bradycardia and hypotension.

– The more potent agents (*bupivacaine*, *ropivacaine*, *etidocaine*) cause malignant ventricular dysrhythmias that are resistant to treatment.

    ○ In species where heart rates range from 60 to 180 bpm, *bupivacaine* is considered to be particularly cardiotoxic.
- This is presumably because the time for dissociation of drug from Na^+ channels during diastole is insufficient to allow Na^+ channel recovery and results in persistent channel blockade.
- Since heart rates in horses are considerably slower, the relevance of this mechanism in equine patients is not known.
- Regardless, *bupivacaine*, or any potent local anesthetic, should not be administered IV to any species at any dose.

Blood
    ○ A number of local anesthetics, most notably *prilocaine*, have been associated with development of *methemoglobinemia*, which results from metabolic breakdown products (e.g. ortho-toluidine) capable of oxidizing the hemoglobin molecule.
    ○ Treatment with *methylene blue* may be indicated if oxygen carrying capacity is compromised.

B. Local tissue toxicity

    ○ When applied in excessively high concentrations, all local anesthetics have the potential to be toxic to nerve tissue, especially when administered via the spinal route.
- Reports of adverse neurologic sequelae after subarachnoid administration of *lidocaine*, *chloroprocaine*, *tetracaine* and other agents have been documented in the human literature.
- The etiology of neurologic deficits after spinal anesthesia in people appears to be multifactorial. Hyperbaric local anesthetic solutions, added preservatives (notably *sodium bisulfite*), and patient positioning have all been implicated as contributing factors.

C. Allergic reactions

    ○ Allergic reactions to aminoamide local anesthetics are extremely *rare*.
    ○ Aminoester local anesthetics are metabolized to *para-aminobenzoic acid (PABA) derivatives* which may induce Type I hypersensitivity reactions in a small percentage of patients.
    ○ Added preservatives such as *methylparaben*, which structurally resembles PABA, may also produce allergic skin reactions.

VIII. Local anesthetic agents commonly used in equine practice

- Local anesthetics are most often administered to produce regional anesthesia; however, they may also be administered systemically to supplement analgesia.
- Details regarding specific equine regional anesthetic techniques are provided in Chapters 16–19.

A. Aminoester local anesthetics

Procaine hydrochloride
- o   Has an intermediate onset (10–15 min) and short duration (45–60 min).
- o   A 2% solution has been used for local infiltration, peripheral nerve blocks, and intra-articular anesthesia.
- o   *Lidocaine* and *mepivacaine* have largely replaced *procaine*.

Proparacaine hydrochloride
- o   The local anesthetic of choice for topical corneal anesthesia in horses.
- o   Available as a 0.5% aqueous solution with a 15-minute duration.

B. Aminoamide local anesthetics

Lidocaine hydrochloride
- o   The most commonly used local anesthetic in clinical equine practice.
- o   Rapid onset (5–10 minutes) and intermediate duration (60–90 minutes).
- o   Available as:
  - –   An aqueous solution in various concentrations (0.5–5%) with or without *epinephrine*.
  - –   A gel in concentrations of 2–5%.
  - –   A 10% spray.
  - –   A eutectic mixture in combination with *prilocaine* (EMLA cream, 25 mg *lidocaine* and 25 mg *prilocaine*/g).
  - –   A transdermal preparation.
- o   2% solutions are used for peripheral nerve blocks, intra-articular anesthesia, caudal epidural anesthesia, and occasionally IV regional anesthesia in horses.
  - –   Effective doses for peripheral nerve blocks and caudal epidural anesthesia in horses typically do not exceed 0.2–0.3 mg/kg (i.e. approximately 5–8 ml of the 2% solution in an average adult horse).
- o   A novel use of *lidocaine* involves the systemic administration of the drug (1.5–2.5 mg/kg IV followed by a continuous infusion of 0.03–0.05 mg/kg/min).
  - –   This technique can significantly decrease anesthetic requirements during surgery, and provide effective analgesia during the postoperative period.
  - –   This protocol does not appear to induce significant effects on cardiovascular function, though further investigation is warranted.
  - –   Studies in human patients indicate that systemic *lidocaine* has a beneficial effect on bowel motility, and this makes it an attractive analgesic adjuvant for the equine colic patient.

Mepivacaine hydrochloride
- o   Is similar to *lidocaine* in its activity profile.
- o   It has a rapid onset (5–10 minutes).
- o   Has a somewhat longer duration than *lidocaine* (120–180 minutes).
- o   A 2% solution is the most commonly used preparation for infiltration anesthesia, intra-articular anesthesia, peripheral nerve blocks and epidural anesthesia.
- o   It is administered at doses similar to those for *lidocaine*.
- o   It is less effective than *lidocaine* for topical anesthesia.

Bupivacaine hydrochloride
- o   Is a potent local anesthetic.
- o   Variable onset (10–30 minutes, depending on the route of administration).
- o   Long duration (180–480 minutes) of action.
- o   It is available as an aqueous solution in various concentrations (0.25–0.75%).
- o   The 0.5% formulation is most commonly used for infiltration anesthesia, intra-articular anesthesia and peripheral nerve blocks in horses.
- o   A 0.5% formulation is used for epidural and subarachnoid administration.
    - –   Doses for peripheral nerve blocks and caudal epidural anesthesia are in the range 0.05–0.08 mg/kg (i.e. 5–8 ml of the 0.5% solution in an average adult horse).
- o   Not effective topically.
- o   Due to its extended duration of action, caution is advised when administering it into the caudal epidural space, as overdose could result in very prolonged periods of hindlimb weakness and motor deficits.
- o   More cardiotoxic than *lidocaine* and IV administration is contraindicated.
- o   Available as a single optical isomer (*levo-bupivacaine*).
    - –   *Levo-bupivacaine* appears to be associated with 30–40% less systemic toxicity on a mg:mg basis.

Ropivacaine hydrochloride
- o   Is a potent local anesthetic.
- o   Variable onset time (10–30 minutes, depending on the route of administration) and a long duration (180–480 minutes).
- o   Like *levo-bupivacaine*, *ropivacaine* is formulated as a single $(S)^{(-)}$ optical isomer and appears to be less toxic than racemic *bupivacaine*.
- o   Available as an aqueous solution in 0.2 and 0.5% concentrations.
- o   Doses are similar to those recommended for bupivacaine.

Etidocaine hydrochloride
- o   Is a potent local anesthetic.
- o   Variable onset time (10–30 minutes, depending on the route of administration) and a long duration (180–480 minutes).
- o   Reported to produce preferential motor block and profound skeletal muscle relaxation.
- o   Not used commonly in horses, and little is known about its effects.

Intravenous lidocaine

- •   Intravenously administered *lidocaine* has anesthetic and analgesic properties.
- •   *Lidocaine* can be administered IV during anesthesia or to the awake horse, or in combination with drugs such as *ketamine* for analgesia.

I. Mode of action

- •   The mechanisms underlying systemic *lidocaine*'s analgesic and anesthetic actions are not fully understood. A number of mechanisms have been proposed:

- A direct action on spinal transmission.
- Attenuation of spontaneous postinjury activity in Aδ and C fibers.
- Blockade of ectopic discharges in neurones involved in nociception.
- Selective block of C fibers.

II. Physiological effects of intravenous lidocaine

- *Lidocaine* has a number of properties which indicate that it may be a beneficial drug to administer in association with general anesthesia or in the awake horse. These include:
  - Analgesia.
  - MAC reduction of volatile anesthetics.
  - Anti-inflammatory actions.
  - Anti-dysrhythmogenic effect.
  - Reduction of risk of postoperative ileus.
  - A protection against endotoxemia (e.g. $\downarrow$ TNFα production).
  - A protection against ischemic and reperfusion injury.
  - Reduction in LPS-induced leucocyte–endothelial cell adhesion.
  - Reduction in LPS-induced macromolecular leakage from vasculature.

III. Metabolism

- *Lidocaine* is metabolized in the liver and produces active metabolites, the most important of which are:
  - Monoethylglycinexylidine (MEGX).
  - Glycinexylidine (GX).

IV. Clinical use of intravenous lidocaine

A. As an adjunct to general anesthetics

- Used with volatile agents to decrease MAC and improve analgesia.
  - Decrease in MAC is dose-dependent.
    - Infusion rates of 50 μg/kg/min reduce MAC by ~ 25%.
    - Infusion rates of 100 μg/kg/min reduce MAC by 40–50%.
- Can be infused concurrently with *ketamine* or alpha$_2$ agonists.
  - MAC $\downarrow$ (60–80%) with *ketamine* (50 μg/kg/min) and *lidocaine* (75 μg/kg/min).

B. To provide analgesia in the awake horse

- Can be safely infused at 50 μg/kg/min for up to 72 h.
  - A loading dose (1.5 mg/kg, IV) can be infused over 5 minutes.
- A dose of 50 μg/kg/min can be safely infused with *ketamine* (0.2 mg/kg/h).

V. Adverse effects

- The likelihood of systemic toxicity with intravenous *lidocaine* is related to its plasma concentration.

A. CNS effects

- ○ Low concentrations of *lidocaine* are sedating.
- ○ Increasing concentrations result in muscle twitching and ataxia.
- ○ The horse may become recumbent temporarily.
- ○ Seizures (originating in *amygdala*) occur at higher doses.
- ○ Administration of sedatives causes a right shift in dose–response curve.
  - – Adverse CNS effects are *unlikely* to occur under anesthesia.

Treatment of seizures
- ○ May use benzodiazepines or *thiopental*.
- ○ Oxygen administration.

B. Cardiovascular effects

- ○ Occur at higher plasma concentrations than do CNS effects.
- ○ Result from a delay in impulse transmission by Na channel blockade. This leads to:
  - – Decreased myocardial contractility.
  - – Vasodilation.
  - – Cardiac dysrhythmias.

Treatment
- ○ Treatment of cardiac toxicity can be unrewarding.
- ○ It is fairly unresponsive to inotropes (e.g. *dobutamine*) and parasympatholytic drugs (e.g. *atropine*).

C. Methemoglobinemia

- ○ Is possible, although clinically significant methemoglobinemia is unlikely with systemic *lidocaine*.
  - – Is much more likely with other local anesthetics such as *prilocaine*.

Muscle relaxants

Elizabeth A. Martinez

- Muscle relaxants may be indicated during equine anesthesia for intraocular or corneal surgery to ensure an immobile eye, during controlled ventilation to prevent 'bucking' of the ventilator, for reduction of displaced fractures, and during certain abdominal procedures (e.g. ovariectomy) to improve surgical exposure.

● When muscle relaxants are administered during general anesthesia, it is imperative to control ventilation, to recognize that the usual indicators of anesthetic depth are abolished (nystagmus, palpebral response, limb movement), and to be vigilant in monitoring neuromuscular function in order to detect, and treat, residual paralysis during recovery.

I. Anatomy and physiology of the neuromuscular junction

A. Release of acetylcholine (ACh)

○ When a nerve impulse arrives at the neuromuscular junction, ACh is released into the junction from synaptic vesicles located in the motor nerve ending.
○ ACh then binds to postjunctional nicotinic cholinergic receptors.

B. Depolarization

○ Occurs when ACh occupies a sufficient number of nicotinic cholinergic receptors.
○ The presence of ACh results in a change in permeability to ions and causes a decline in the transmembrane potential, which triggers a membrane action potential.

C. Action potential

○ The action potential spreads across the surface of the skeletal muscle.
○ This causes calcium (which opposes troponin-induced inhibition of muscle contraction) to be released from the sarcoplasmic reticulum into the sarcoplasm.
○ Myosin is free to interact with actin, and the muscle fiber contracts.

D. Repolarization

○ Occurs when ACh diffuses away from its receptor and is metabolized by acetylcholinesterase.
○ The rapid hydrolysis of ACh prevents sustained depolarization.

II. Pharmacology

● Muscle relaxants are classified into *depolarizing* and *nondepolarizing* agents.
○ Depolarizing muscle relaxants mimic the action of ACh.
○ Nondepolarizing muscle relaxants compete with ACh for binding sites.

III. Depolarizing muscle relaxants

● *Succinylcholine* is the only depolarizing agent in clinical use.

A. Mode of action of succinylcholine (SCh)

- ○ Acts by binding to ACh receptors in the same way as does ACh, causing initial muscle fasciculations followed by sustained depolarization (*phase I block*).
- ○ A *phase II block* occurs following prolonged exposure to SCh.
  - The characteristics of a phase II block resemble a non-depolarizing block.

B. Onset of action of succinylcholine

- ○ SCh has a rapid onset and duration of action.
- ○ In *halothane*-anesthetized horses, a loading dose of 0.33 mg/kg IV, followed by an infusion at 2.2 mg/kg/h, provides adequate muscle relaxation.

C. Adverse effects

- ○ Hyperkalemia.
- ○ Myalgia (may be related to muscle fasciculations).
- ○ Cardiac dysrhythmias.
- ○ Increase in intracranial, intraocular, and intragastric pressures.

D. Termination of effects

- ○ Is due to hydrolysis by *plasma cholinesterase*.
- ○ Prolonged duration of action of SCh occurs with decreased plasma cholinesterase activity.
  - Organophosphate treatment, malnutrition, anemia, pregnancy, and hepatic disease have been shown to decrease plasma cholinesterase activity.

E. Misuse of succinylcholine

- ○ Using SCh as the sole agent for immobilization of horses is **inhumane** since SCh does not have anesthetic or analgesic properties.

IV. Nondepolarizing muscle relaxants

A. Atracurium (0.08–0.1 mg/kg, IV)

- ○ Short onset of action.
- ○ Duration of action is dose-dependent (~15–20 min).
- ○ The duration of action is increased by either giving a larger initial dose or by giving one-third to one-half of the initial dose as a repeat bolus.
- ○ Termination of effects is from Hofmann elimination (pH- and temperature-dependent spontaneous degradation) and ester hydrolysis.
- ○ Cardiovascular effects are minimal.
- ○ Shown to cause histamine release with resultant hypotension and tachycardia.
  - Clinical signs of histamine release have *not* been observed in horses given appropriate doses.
  - Nevertheless, large doses should be administered slowly.

○ *Laudanosine*, a metabolite of *atracurium*, is a cerebral stimulant. However, this is not clinically significant when appropriate doses of *atracurium* are used.

B. Cisatracurium

○ A dose has not been described for the horse.
○ Approximately one-fifth as potent as *atracurium*.
○ It is a stereoisomer of *atracurium*.
○ At equipotent doses, *cisatracurium* has a similar onset and duration of action as *atracurium*.
○ Undergoes Hofmann elimination.
○ Does *not* exhibit histamine release (in contrast to *atracurium*).
○ May be attractive choice because it combines the non-organ elimination of *atracurium* with the cardiovascular stability of vecuronium.

C. Pancuronium (0.12–0.18 mg/kg, IV)

○ No histamine-releasing action.
○ Vagolytic action, which can result in hypertension and tachycardia.
○ Undergoes hepatic metabolism and renal elimination.
○ In horses, compared with other species, *pancuronium* is relatively impotent.
 – Higher doses than are typically used in other species are required to produce acceptable muscle relaxation.
 – For this reason, *pancuronium* is impractical and cost-prohibitive in most instances.

D. Vecuronium

○ Closely related to *pancuronium* but with a shorter duration of action.
○ Lacks significant cardiovascular effects.
○ Recovery is the result of hepatic metabolism and renal excretion.
○ Due to its similarity to *pancuronium*, the same disadvantages exist with regard to its lack of potency and requirement for higher doses compared with other species.

E. Mivacurium

○ A short-acting muscle relaxant that is hydrolyzed by plasma cholinesterase.
○ At higher doses, histamine release may cause hypotension.
○ Recovery may be prolonged if plasma cholinesterase activity is reduced.

F. Miscellaneous drugs

○ Including *doxacurium*, *pipecuronium*, *rapacuronium*, and *rocuronium*.
 – Little clinical data are available for the horse.
○ When evaluating a newer muscle relaxant for clinical equine anesthesia, one must consider its onset and duration of action, method of elimination, cost and its potential for unwanted cardiovascular effects.

V. Factors affecting neuromuscular blockade

A. Impaired metabolism and elimination

○ Abnormal hepatic or renal function can prolong the duration of, and recovery from, neuromuscular blockade if the particular muscle relaxant is dependent on organ function for metabolism and/or elimination.

  – *Atracurium* and *cisatracurium* rely partly on Hofmann elimination, and therefore clinical recovery is less affected by organ dysfunction.

B. Drug interactions

○ Volatile anesthetics, commonly used anesthetic induction agents (e.g. *ketamine*, *thiopental*), and benzodiazepines cause a dose-dependent potentiation of muscle relaxants.

○ Certain medications given concurrently with muscle relaxants can affect the degree and duration of neuromuscular blockade, as well as prolonging the recovery time.

  – *Gentamicin*, an aminoglycoside antibiotic, has been shown to potentiate the clinical effect of *atracurium* in anesthetized horses.

VI. Monitoring and antagonism of neuromuscular blockade (see Chapter 14)

Non-steroidal anti-inflammatory drugs (NSAIDs)

- NSAIDs are widely used in equine practice, especially for treating pain and inflammation resulting from musculoskeletal injuries, and as analgesics in the surgical patient.
- Historically, extracts of willow bark were used to treat fever.
- The active ingredients were isolated leading to the therapeutic use of *salicylates*.
- However, it was only relatively recently that the mode of action of salicylates was elucidated and their role in blocking prostaglandin (PG) formation was described.

I. Prostaglandins

- Products of arachidonic acid, called eicosanoids, were first described in the 1930s after reports that semen contained a substance which contracted uterine smooth muscle.
- The active substance was thought to originate in the prostate, hence prostaglandin.
- Several more prostaglandins were found to be generated in tissues.
- In the early 1970s it was postulated that inhibition of prostaglandin synthesis was the mechanism of action of aspirin-like drugs.

II. Arachidonic acid

- Arachidonic acid (20-carbon atom) is esterified in the phospholipids in the cell membrane.

- The initial and rate-limiting step in the synthesis of eicosanoids is the liberation of arachidonic acid from the cell membrane.
- A variety of stimuli can liberate arachidonic acid.
- Cell damage, from any cause, can initiate the process.

A. Release of arachidonic acid

- Can involve a one-step or two-step process.
  - The one-step process involves phospholipase A_2.
  - The two-step involves phospholipase C and diacylglycerol or phospholipase D and phospholipase A_2 (PLA_2).

B. Metabolism of arachidonic acid

- Free arachidonic acid is metabolized by a variety of pathways.
  - For example, fatty acid cyclooxygenases (COX) initiate the synthesis of prostaglandins and thromboxanes.
- Various lipoxygenases are responsible for the synthesis of leukotrienes.
- NSAIDs inhibit COX activity and thus decrease synthesis of prostanoids.
- Most clinically used NSAIDs do not affect lipoxygenase enzymes.
- Corticosteroids inhibit the lipoxygenases and cyclooxygenase pathways by blocking the release of PLA_2.

III. Cyclooxygenase enzymes (COX)

- Cyclooxygenase (COX) exists in two isoforms: COX-1 and COX-2.
- Different genes encode COX-1 and COX-2.
- A third cyclooxygenase (COX-3) has been proposed as the central site of action of *acetaminophen*.

A. COX-1

- COX-1 is the *constitutive* form and is involved in PG synthesis in various organs.
- Therefore, COX-1 is important for maintaining normal physiologic functions:
  - Cytoprotective PGs are important in the stomach.
  - PGs are responsible for blood flow regulation in the kidney, especially in *low-flow* states.
  - Platelet function (only COX-1 is expressed in platelets).
- Inhibition of COX-1 results in toxic effects (e.g. gastric ulceration)

B. COX-2

- The *inducible* form is induced by inflammation.
- Normal concentrations are low.
- Expression is short-lived.
- COX-2 expression is inhibited by NSAIDs and glucocorticoids.

○ NSAIDs selective for COX-2 have fewer toxic side effects.
 – However, COX-2 also appears to have *constitutive* functions, as long-term use of COX-2 selective NSAIDs has been associated with toxicity.

C. COX-3

○ Has been proposed as a variant of COX-2 based on the findings that:
 – COX-3 can be induced with high concentrations of NSAIDs.
 – It is highly sensitive to inhibition by *acetaminophen*.
○ It may be a product of the same gene that encodes COX-2.
○ *However, recent evidence casts doubt on the existence of COX-3*.

IV. Clinical actions of NSAIDs

• Most NSAIDs in clinical use inhibit COX-1 and COX-2 isoforms.
• NSAIDs differ markedly from one another in chemical structure, but most have three major types of effect:
 ○ Anti-inflammatory.
 ○ Analgesic.
 ○ Antipyretic.

A. Anti-inflammatory effects

○ Are linked to inhibition of *prostanoid* production.
○ Prostanoids are an integral part of the inflammatory process and the predominant product is PGE_2, though PGI_2 is present in small amounts.
○ In *acute inflammation*, PGE_2 and PGI_2 are released from local tissues and blood vessels, and PGD_2 is released from mast cells.
○ In *chronic inflammation*, monocytes and macrophages also generate PGE_2.
○ During inflammation, the prostanoids have a synergistic action with bradykinin and histamine to induce a powerful vasodilation.
 – Hence the redness in areas of acute inflammation.
○ NSAIDs ameliorate the effects of endotoxin-induced inflammation.

B. Analgesic actions of NSAIDs

Peripheral effects
○ The analgesic effects of NSAIDs are generally attributed to their effects on *prostanoid* formation.
○ While not directly involved in inducing pain, many PGs sensitize nociceptive afferent nerve endings to chemical mediators (e.g. histamine, 5HT, bradykinin).
○ NSAIDs are most effective in treating pain of inflammatory origin (e.g. osteoarthritis).
○ In the postoperative period, NSAIDs provide mild to moderate analgesia.
 – NSAIDs may increase the efficacy of more potent agents such as opioids.
○ *Ketoprofen* may have an *anti-bradykinin* action.

Central effects

o NSAIDs produce analgesia when injected into the spinal canal.
  – This indicates that PGs have a role in the conduction of noxious stimuli in the spinal cord.
o A central analgesic action has been described for NSAIDs.
  – NSAIDs, especially *ketoprofen*, cause the formation of a naturally occurring substance, *kynurenic acid*, which inhibits transmission of noxious stimuli.
    ■ Kynurenic acid antagonizes excitatory amino acids in the mammalian brain.
  – NSAIDs increase the activity of the hepatic enzyme *tryptophan 2,3-dioxygenase* which catalyses the conversion of tryptophan to kynurenic acid.

C. Antipyretic effect

o The antipyretic effect of NSAIDs is thought to be due to the inhibition of prostaglandins in the hypothalamus.
  – Endotoxins cause the release of interleukin-1 (IL-1) from macrophages, and it is thought that IL-1 causes the generation of E-type PGs in the hypothalamus, which in turn cause an increase in the temperature setpoint.
o There may also be other mechanisms involved in fever control by NSAIDs.

V. Toxic effects of NSAIDs

● The severity of adverse effects is related to dose and duration of treatment.
● Concomitant use of other potentially toxic drugs may synergistically act with NSAIDs to promote toxicity.
  o An example of the latter is the increased incidence of renal damage with concurrent use of tetracyclines.

A. Gastrointestinal toxicity

o Gastric ulceration and right dorsal colitis are generally a result of chronic use of NSAIDs. Gastric ulceration and bleeding may arise from:
  – An effect of acid secretion (PGs decrease acid secretion from parietal cells).
  – Disruption of the mucosal barrier.
  – Interference with mucosal blood flow.
o *Misoprostol*, a PG analogue, prevents NSAID-induced gastric damage, indicating that PG inhibition has a role in the toxicity of NSAIDs.

B. Renal toxicity

o Is a risk with NSAID use, especially in hypotensive states.
o Is related to inhibition of PG synthesis (PGE_2 and PGI_2).
  – Prostaglandins are involved in the regulation of renal blood flow, especially under *low-flow* situations (e.g. during shock or anesthesia-induced hypotension).
o The potential for renal damage is increased if NSAIDs are combined with other nephrotoxic agents.
o The horse seems to be less susceptible to renal damage than other species.

C. Hemostasis

o Interference with clotting (platelet inhibition; see Chapter 8).
o Does not appear to be a significant problem in the horse.
  – NSAIDs are widely used in surgical patients and clinically significant clotting problems are rare.

Drugs used in endotoxemia

- Endotoxemia is present in at least 40% of horses undergoing emergency abdominal surgery for gastrointestinal problems.
- Lipopolysaccharide (LPS), a major component of the outer membrane of Gram-negative bacteria, evokes a variety of biological responses.
- The horse is among the most sensitive of animals to the toxic effects of LPS.
  o Only man and the chimpanzee are more sensitive than the horse to LPS.

I. Treatment of endotoxemia

- Treatment is aimed at:
  o Cardiovascular support (fluids, inotropes).
  o Reducing the release and/or effects of cytokines.

II. Drugs used in treatment of endotoxemia

A. Non-steroidal anti-inflammatory agents (NSAIDs)

o Effective in blocking the clinical effects of LPS.
o Decrease the production of prostaglandins by inhibiting LPS-induced COX enzyme induction in a variety of tissues.
o NSAIDs, except *phenylbutazone*, inhibit the production of nuclear factor κB (NFκB), which is important in cytokine gene transcription.

B. Polymixin B (PB)

o *PB*, a polypeptide antibiotic, is not used as an antimicrobial due to its nephrotoxicity at therapeutic doses.
o Even at sub-therapeutic doses, *PB* has a high affinity for lipid A, the common component of LPS molecules.
o *PB* reduces the adverse effects of LPS in horses and reduces cytokine production.
o The effects of *PB* are dose-related.
  – Doses of 1000–6000 IU can be administered presurgery or intraoperatively.
  – *PB* is usually diluted (1 liter 0.9% NaCl) and infused slowly (~ 15 minutes).

C. **Dimethyl sulphoxide (DMSO)**

- o Has been proven to have anti-inflammatory actions and to be efficacious in experimental models of endotoxic shock.
- o *DMSO* decreases cytokine production (e.g. ↓ TNFα production).
- o Doses of up to 1 g/kg, IV, are used daily.
  - – High concentration can cause hemolysis.
  - – Overdose can result in pulmonary edema.
  - – Lower doses (~ 0.2 g/kg, IV) are safer and may be as beneficial.
- o Dilute in a large volume (3–5 liters) of balanced electrolyte solution for infusion.
- o *DMSO* has human health hazards.
  - – Hospital personnel must take precautions when using *DMSO* (e.g. gloves).
- o *DMSO* is excreted mainly (~70%) via the lungs, so good ventilation is important to avoid inhalation by hospital personnel.

12   The anesthetic machine

I. Anesthetic gases

A. Oxygen (O_2)

- *Oxygen* is the principal gas used in equine anesthesia.
  - *Nitrous oxide* (N_2O) is rarely used in equine anesthesia.
- Cylinders are the usual source of O_2.
  - Attached to the machine (E type) or remotely situated larger cylinders (H type).
- In certain hospital situations, O_2 may be supplied by pipeline from a liquid O_2 source with the E cylinders on the machine as a backup.
- O_2 in cylinders is entirely in the gaseous form (in contrast to N_2O).
- The volume of O_2 in an E cylinder can be estimated by multiplying the pressure (psig) by 0.3. (*psig* refers to pounds per square inch gauge and is the difference between the measured pressure and atmospheric pressure. Most gauges are calibrated at an atmospheric pressure of zero).
  - A full E cylinder has a volume of 600 liters (2000 psig $\times$ 0.3 = 600).
- The volume of O_2 in an H cylinder can be estimated by multiplying psig by 3.

B. Pressure regulation

- To maintain a constant flow, it is necessary to regulate the O_2 pressure leaving the cylinder.
- A pressure-reducing valve, placed downstream from the O_2 cylinder, reduces the pressure to about 45 psig.
- On more sophisticated machines, a second pressure-reducing valve reduces the pressure further (to 15–25 psig).
- Pipeline O_2 pressure is ~ 50 psig.

II. Flow meters

- Flow meters direct the O_2 flow from the regulator to the vaporizer.
- Flow meters accurately measure gas flow.
  - Flow rate is indicated by a small metal ball or rotating float (bobbin) in the calibrated flow tube.
- Flow in the tube is a function of physical properties (viscosity and density) of the gas.
  - *Viscosity* is the primary factor at low flows.
  - *Density* is the primary factor at high flows.

- For safety, when using more than one gas (e.g. N_2O and O_2):
    o The flow meters and adjusting knobs are color-coded.
    o The O_2 flow meter is positioned immediately before the common gas outlet.
        – This feature decreases the likelihood of a hypoxic gas mixture being delivered in the event of leaks in the system.
- Two oxygen flow meters are present on some machines.
    o One is used for flows up to 1 liter/min and the other for flows >1 liter/min.
    o This allows more precise delivery of O_2.
    o This feature is not present on machines designed for full-size horses.

III. Vaporizers

- *Vapor* describes the gaseous state of agents which are liquid at room temperature.
- The roles of the vaporizer are to *store* the liquid anesthetic and *deliver the desired volume* of the anesthetic vapor to the fresh gas flow.
- *Capacity* of a vaporizer refers to the maximum concentration that can be delivered at the highest setting of the dial.

A. Classification of vaporizers

Regulation of output concentration
    o Modern vaporizers are of the *variable bypass* design.
    o Fresh gas entering the vaporizer is split into two streams:
        – A smaller *carrier* portion that passes through the vaporizer.
        – A larger *bypass* portion that exits the vaporizer without contacting the anesthetic.
    o Upon exiting the vaporizer, both streams mix to give the concentration set on the control dial.

Method of vaporization
    o Modern vaporizers are of the *flow-over* design.
    o The carrier gas enters a vaporizing chamber and becomes saturated with the anesthetic.

Location in the circuit
    o Modern vaporizers are located out-of-circuit (i.e. not in the breathing circuit).

Temperature compensation
    o Modern vaporizers are temperature compensated.
    o Temperature compensation is achieved by either:
        – A bimetal strip in the bypass gas flow.
        – A gas-filled bellows that controls a bypass valve.

Agent specificity
    o Modern vaporizers are designed for use with a single volatile anesthetic.

Desflurane vaporizer
    o This system is specially designed for *desflurane* which has a high vapor pressure (664 mmHg at 20°C).

     ○ The vaporizer is sealed from the atmosphere and pressurized (1550 mmHg).
     ○ The vaporizer is electrically heated (23–25°C).
     ○ These modifications are designed to reduce the volatility of *desflurane*.

B. Hazards of vaporizers

     ○ Use of (i.e. filling with) incorrect anesthetic.
     ○ Entry of liquid anesthetic into the bypass chamber if the vaporizer/machine is tipped over.
         – This could result in dangerously high concentrations in the inspired limb.
     ○ Leaks (e.g. if the filler cap is loose).

C. Estimating the volume of liquid anesthetic used

     ○ An estimate of the volume of liquid used can be made from the equation:

> Total volume (ml) = 3 × dialed % × fresh gas flow (liters/min) × hours
> (*3 is a factor used to correct for time and volume units.*)

    Example: *Isoflurane* (2%) at 5 liters/min for 1.5 hours.
              Volume of isoflurane = 3 × 2 × 5 × 1.5 = 45 ml.
     – This equation shows the influence of fresh gas flow on the output of anesthetic from the vaporizer.

IV. Anesthetic circuits

● The function of a circuit is to deliver oxygen and anesthetic and to remove CO_2.
● The circuit is positioned between the common gas outlet of the anesthetic machine and the horse.
● There are three systems available:
     ○ Circle systems (rebreathing systems) are used in horses.
     ○ To-and-fro systems (rebreathing systems) are used less commonly.
     ○ Non-rebreathing (e.g. Bain) systems are not used in horses due to the high fresh gas flow needed to remove CO_2 (~ 100 ml/kg/min during controlled ventilation).

A. Circle system (see Fig.12.1)

     ○ Consists of the following components:
         – Fresh gas inflow.
         – Inspiratory and expiratory unidirectional valves.
         – Two corrugated tubes forming the inspiratory and expiratory limbs.
         – A Y-piece connecting the corrugated tubes to the endotracheal tube.
         – A reservoir bag.
         – A pop-off (overflow) valve to allow venting of gases from circuit.
         – A soda lime canister and CO_2 absorbent.
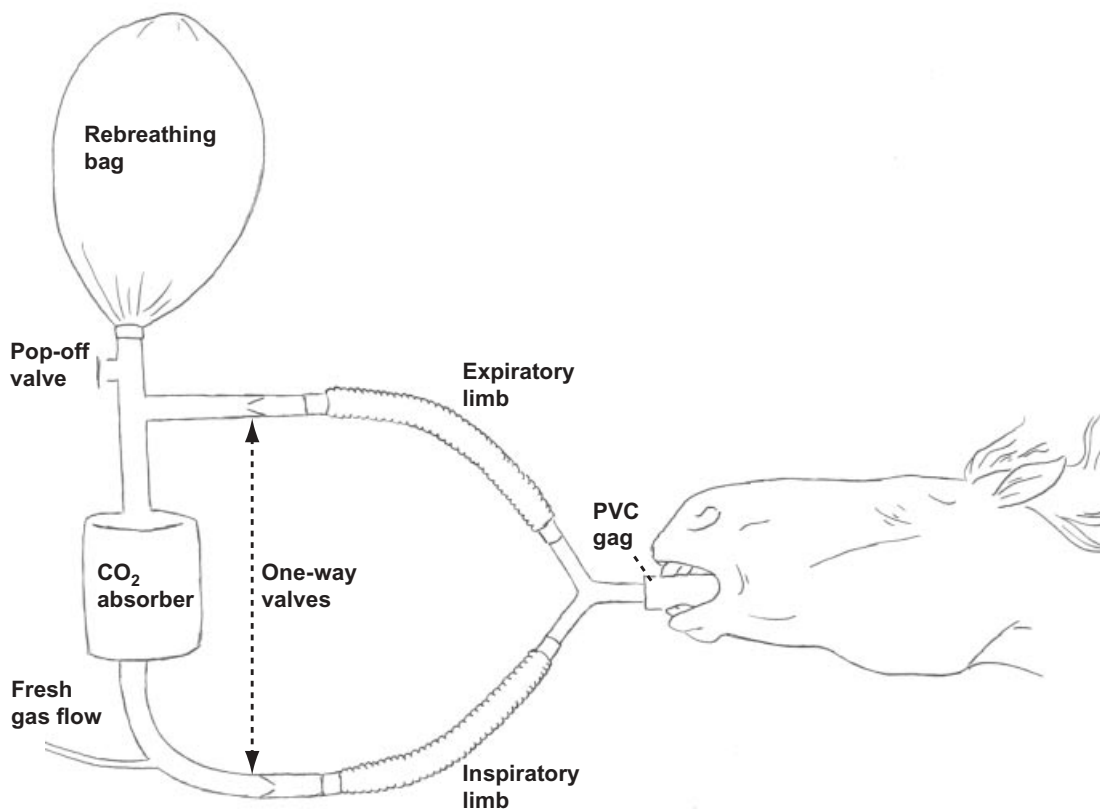
Fig. 12.1   Schematic representation of a circle system.

B. To-and-fro system (see Fig. 12.2)

- o   Has never been popular in North America and is rarely used nowadays.
- o   Has no unidirectional valves or breathing tubes.
- o   The endotracheal tube is connected *directly* to the system, very close to the soda lime canister (to reduce dead space).
- o   Exhaled gas moves through the soda lime into the rebreathing bag and from the rebreathing bag back through the soda lime to the horse on inspiration (*to-and-fro*).
- o   The soda lime in the bottom of the canister gets used up first and this contributes to 'channeling' and an increase in dead space.
- o   *Advantage*:
  - –   The system is portable.
- o   *Disadvantages*:
  - –   The canister is located close to the endotracheal tube, and this can make it difficult to position and support, especially with a horse in dorsal recumbency.
  - –   The risk of inhaling soda lime dust is greater with this system.
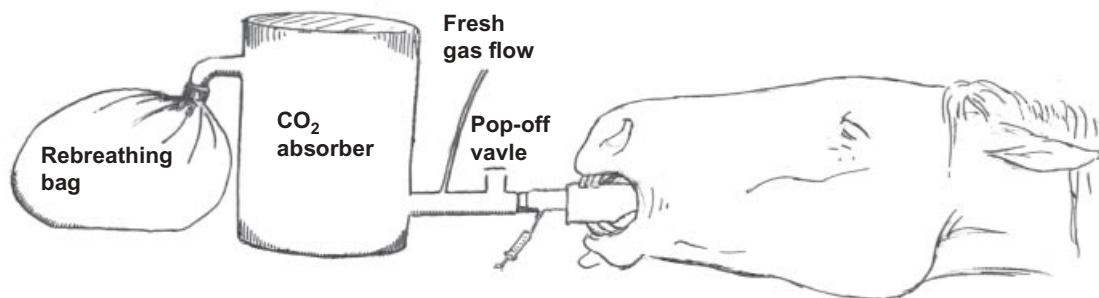
Fig. 12.2   Schematic representation of a to-and-fro system.

C. Carbon dioxide (CO_2) absorption

- o CO_2 is removed from the circuit by a chemical reaction with soda lime or *Baralyme* (barium hydroxide lime).
- o   Heat and water are byproducts of these reactions.
- o   *Indicators* (e.g. ethyl violet) are added to the absorbent and change color as the absorbent becomes exhausted.

Reaction of CO_2 with soda lime

$$CO_2 + H_2O \rightarrow H_2CO_3$$
$$H_2CO_3 + 2NaOH\ (KOH) \rightarrow Na_2CO_3\ (K_2CO_3) + 2H_2O + Heat$$
$$Na_2CO_3\ (K_2CO_3) + Ca(OH)_2 \rightarrow CaCO_3 + 2NaOH\ (KOH)$$
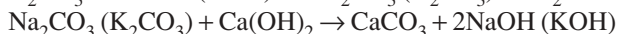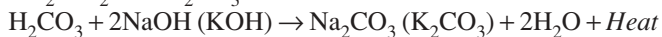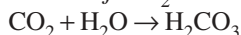
Reaction of CO_2 with Baralyme

$$Ba(OH)_2 + 8H_2O + CO_2 \rightarrow BaCO_3 + 9H_2O + Heat$$
$$9H_2O + 9CO_2 \rightarrow 9H_2CO_3$$
$$9H_2CO_3 + 9Ca(OH)_2 \rightarrow CaCO_3 + 18H_2O + Heat$$
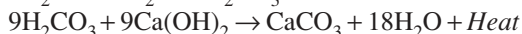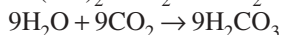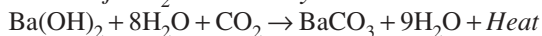
D. Inspired anesthetic concentration in a circle system is affected by the following

- o   The volume of the system.
  - –   ~ 50 liters for a large animal machine.
- o   The fresh gas flow.
  - –   The higher the flow the more anesthetic delivered per minute.
- o   The concentration of anesthetic in fresh gas flow.
  - –   Dependent on vaporizer setting.
- o   Uptake of anesthetic by the horse.
  - –   Dependent on factors such as solubility of anesthetic and body mass of horse.
- o   Uptake of anesthetic by the system.
  - –   e.g. Reaction with rubber components and soda lime.
- o   Elimination (e.g. N_2, CH_4) and uptake (e.g. N_2O) of other gases by the horse.

V. Ventilators

- Most modern anesthetic machines for adult horses have a ventilator incorporated in the design.
- Ventilators are driven by electrical power, compressed gas, or both.
- To connect the ventilator on most systems, the reservoir bag is removed and the circuit is completed by attaching the reservoir bag mounting to a bellows (using a length of tubing) housed inside a plastic chamber.
  - Some small animal machines, primarily those designed for human patients, have a *selector switch* which allows this maneuver to be performed without removing the reservoir bag.
- The chamber is pressurized using a *driving gas* (O_2 or compressed air), causing the bellows to empty.
  - It is desirable to use O_2 as the driving gas, because a leak in the bellows could result in a hypoxic mixture being delivered if compressed air enters the bellows.
  - The driving gas is vented from the chamber during expiration.
- Most modern ventilators are *time-cycled*.
- *Safety*:
  - A ventilator with a bellows that *descends during inspiration* is safest, because the bellows will collapse when empty and is easily detected.

A. Hazards of ventilator use

- System connected incorrectly.
- Use of excessive driving pressure.
- Leaks in the bellows.
  – Especially important when compressed air is the driving gas.
- Malfunction in the relief valve resulting in excessive airway pressure.
- Failure to empty the bellows.
  – Malfunction in the driving system.
  – Failure to empty an *ascending* bellows can also be caused by a leak in the bellows.

B. Weaning the horse off the ventilator

- Generally not a problem in horses that have not had neuromuscular blockers.
- The time to return of spontaneous ventilation is influenced primarily by the anesthetic regimen and depth of anesthesia.
  – Hypothermia will delay awakening and return to spontaneous breathing, but this is more likely to occur in *foals*.
- *There is no point in attempting to make a horse breathe spontaneously if it is deeply anesthetized*.
  – Physical (e.g. ear twisting) or chemical stimulation (e.g. *doxapram*) is discouraged.
  – Allowing the $PaCO_2$ to increase and act as a respiratory stimulant is discouraged, as it will be ineffective if the horse is in a deep plane of anesthesia and may lead to hypoxemia.
  – The most important maneuver is to *decrease the depth of anesthesia* in preparation for the return of spontaneous respiration.

o   When spontaneous breathing resumes, the initial tidal volumes are low and should be supplemented by controlled ventilation, at a reduced rate, using the anesthetic machine or a *demand valve*.
   –   A demand valve is especially useful if the horse is moved into the recovery area prior to the resumption of spontaneous breathing.
   –   A demand valve can be driven by a pipeline oxygen system (~ 50 psig) or from an oxygen cylinder regulated to a pressure of 50–70 psig (for adults).
      ■   Use a pressure < 50 psig in foals to prevent overinflation of the lungs.

VI. Scavenging of anesthetics

●   Involves the removal from the surgical suite of anesthetic vapors vented from the anesthetic machine.
●   A scavenging system is necessary to protect personnel from exposure to potentially harmful compounds.
●   Scavenging systems can be *passive* or *active*.
   o   *Passive systems* direct the vented gases and vapors away from the machine using relatively wide-bore tubing.
      –   This method is *not very efficient* as the vented gases may get redirected back into the surgical suite due to air currents or leaks.
   o   *Active systems* involve the use of a negative pressure to evacuate the vented gases.
      –   This system is more efficient but must be installed properly to avoid creating a hazard.

VII. Scavenging interfaces

●   Use of scavenger interfaces protects the breathing circuit and the patient's lungs from excessive positive or negative pressure.
●   Interfaces consist of three components:
   o   Positive pressure relief.
   o   Negative pressure relief.
   o   A reservoir.
●   If the scavenging system outlet becomes occluded, the positive pressure relief vent opens to prevent transmission of high pressure to the breathing circuit.
●   If an *active* disposal system is used, a negative pressure relief is needed to prevent negative pressure (suction) from the disposal system reaching the patient's breathing circuit.
   o   Excessive negative pressure can remove oxygen from the system. In extreme cases, lung collapse could result.
   o   To avoid this occurrence, the scavenging system should have a port to allow air to be entrained and avoid the build-up of excessive negative pressure.
●   A *reservoir* is necessary to allow the scavenging system to accommodate an increased volume of excess anesthetic gas which may transiently exceed the removal capacity (liters/min) of the system.
   o   A rebreathing bag of appropriate size (~ 3 liters), is used as a reservoir.

A. Open interface

- o An open interface is always open to the atmosphere and contains no valves.
- o Open interfaces should be used only with *active* systems.
- o A hissing noise from an open interface is normal.
- o While safer for the patient (no hazard of positive or negative pressure being applied to the airway as a result of scavenger failure), the risk of occupational exposure is higher.

B. Closed interface

- o A closed interface communicates with the atmosphere by use of spring-loaded or weighted valves for positive and negative pressure relief.
- o The vacuum should be adjusted so that the reservoir bag is neither flat nor overdistended.
- o A positive pressure relief is always required to allow release of gases into the room in case of obstruction of the scavenging system downstream of the interface.
- o If an *active* disposal system is used, a negative pressure relief valve is also necessary to allow entrainment of room air when the pressure falls below atmospheric.

13   Positioning the anesthetized horse

Hui Chu Lin

I. Introduction

- Normal horses spend most of their time standing.
- Horses normally spend only short periods of time (~ 30 minutes) in recumbency.
  - Recumbency likely becomes uncomfortable due to pressure on muscles and the skeletal system.
  - The large body mass of the horse means that dependent structures undergo considerable forces.
  - Horses do not normally spend time in dorsal recumbency.
- Every effort must be made to ensure that the effects of posture are minimized in the anesthetized horse.

II. Problems associated with recumbency

- May impose significant *cardiovascular and pulmonary changes*, particularly over prolonged periods.
- *Myopathy* can result from ischemia.
  - Arterial supply is compromised and venous drainage decreased due to compression of blood vessels in dependent muscles.
  - Generally manifests as unilateral forelimb lameness (triceps myopathy) following lateral recumbency.
  - Bilateral hindlimb lameness may occur following dorsal recumbency.
  - Especially significant with heavy, muscular horses in the presence of a low arterial blood pressure.
- *Neuropathy*, especially of peripheral nerves, can result from pressure on the nerve or stretching the nerve.

III. Preventing complications in lateral recumbency (see Figs 13.1 and 13.2)

A. Padding

- A thick *foam* pad works well, but *water* or *air* cushions may also be used.
  - Foam padding should be about 10–12 inches (25–30 cm) thick and covered with a waterproof material.
  - Air cushions should be inflated to the point at which the horse is just lifted off the table.
  - Air and water cushions have the disadvantage of creating an unsteady platform, and water cushions in particular create a '*rocking*' movement.
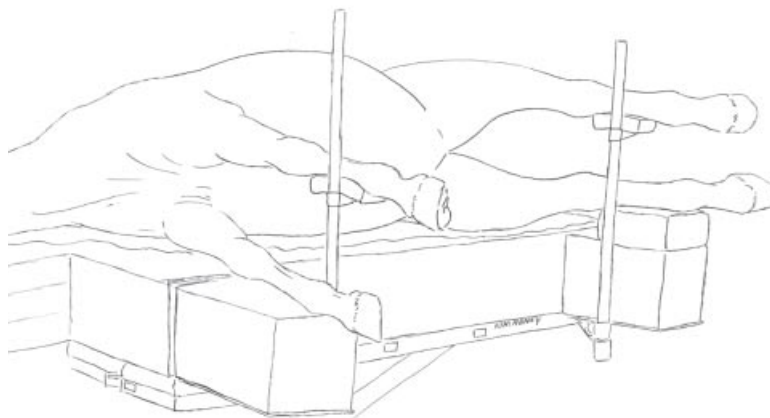
Fig. 13.1   Schematic representation of a horse in lateral recumbency showing the lower thoracic limb pulled forward.
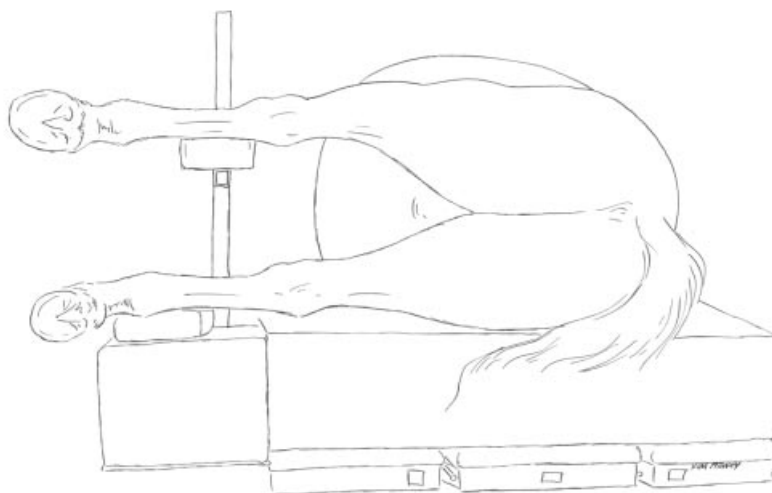
Fig. 13.2   Schematic representation of a horse in lateral recumbency. The hind quarters should not extend beyond the edges of the padding and the upper limbs are supported parallel to the table top.

○   Covering the pad with a blanket or towels absorbs sweat and fluids which may accumulate during surgery and helps to keep the horse dry.

B. Positioning

○   It is imperative that the *entire body* is situated on the padding.
○   Avoid having the extremities too close to or over the edge of the mat.
○   The *head* should be placed in a neutral position, avoiding overflexion or overextension.
○   Halters should be removed to prevent pressure-induced trauma, especially to the facial nerve.

o   The *eyes*, especially the lower eye, should be protected.
  –   The lids on the lower eye should be closed and care taken to protect the eye if the head is 'dragged' along the mat during positioning.
  –   Sterile lubricant should be placed on the eyes and repeated, if necessary, during long procedures.
o   The *tongue* should be placed so as to prevent pressure damage.
  –   This usually involves placing the tongue uppermost and withdrawing it from the mouth.
  –   The tongue should be covered with moist towels to prevent drying.
o   Check that the dependent *ear lobe* is not trapped under the head.
o   The *limbs* need special attention.
  –   The *lower thoracic* limb should be pulled forward to protect the triceps from the pressure of the chest wall.
    ■   Avoid pulling the lower thoracic limb backwards.
  –   The *upper limbs* should be supported in a position parallel to the tabletop, using either specific leg attachments, designed for the table, or padding.
    ■   It is preferable *not* to place support pads for the upper limbs on top of the lower limb.
  –   A space should be left between the adductors of the *pelvic limbs* to avoid muscle damage.
o   Check that the *penis* is not trapped under the body.
o   Check that the bony part of the *tail* is not placed under the body.
o   Tilting the laterally recumbent horse (by raising the limbs with hobbles and a hoist) to reduce pressure on the lowermost musculature is likely to transfer pressure to the hip and shoulder regions and is *not* recommended.

IV. Preventing complications in dorsal recumbency

A. Padding

o   Thickness will be dictated by the design of the surgical table.
  –   With many surgical tables, it is only possible to use a 3–5 inch (7.5–12.5 cm) pad.
o   Supporting the horse by hobbles and an overhead hoist allows use of a thicker pad.
o   The thickness of the pad is less critical for dorsal recumbency, provided that the horse is positioned squarely on its back.

B. Positioning

o   The horse should be placed squarely on its back.
o   Avoid having the *croup* overhang the padding.
o   The horse can be maintained in dorsal recumbency either by the use of hobbles and an overhead hoist or, more commonly, from a 'V' support formed by folding the table.
o   The *shoulder* area should be well padded.
o   The *thoracic limbs* may be allowed to rest on the sternal area if not supported from overhead, but some padding may be needed on the sternum especially if the horse has heavy shoes.

- o The *pelvic limbs* may be allowed to relax in the flexed position if not supported from overhead, depending on the facilities and the surgery in question.
  - – It is important to *avoid long periods with the pelvic limbs in extension* as this increases the likelihood of femoral nerve damage and recovery problems.
- o The bony part of the *tail* should not be placed under the horse or between a rear limb and the padding.
- o The *head* should be aligned with the body and padding placed under the poll.
  - – Overextension of the head and neck should be avoided by placing a wedge-shaped pad under the nasal bones.
  - – Overextension may increase the risk of *recurrent laryngeal nerve* damage.
  - – Removal of the halter is less critical if the horse is dorsal; if not removed, it should be checked to ensure that it is not too tight.
- o The *eyes* should be protected from trauma, which may occur if a V-shaped head support is used.
- o Check that the *ears* are not trapped under the poll.

14 Monitoring the anesthetized horse

Monitoring the central nervous system

Joanna C. Murrell

- General anesthesia can be defined as a reversible state of depression of the central nervous system (CNS) of such a degree that consciousness is lost and that on recovery nothing relating to the period of anesthesia is recalled.
- CNS monitoring is an inherent part of anesthetic monitoring and is intricately linked to monitoring the depth of anesthesia.
- The need to quantify the depth of anesthesia in man, to prevent overdose, was identified in 1848 by John Snow.
  - This system was later modified to produce a more sophisticated assessment of anesthesic depth.
- Attention has focused on the EEG as a monitor of anesthetic depth in the horse.
  - This interest in EEG studies probably reflects the relatively high anesthetic mortality rate in horses and the dose-dependent cardiovascular and respiratory effects of anesthetic agents.

I. Awareness during anesthesia

- In the early days of anesthesia, patient awareness during surgery was uncommon. Rather, morbidity and mortality during anesthesia were more likely due to the patient being 'too deeply' anesthetized.
- The introduction of muscle relaxants into human clinical practice in 1942 created the potential for the patient to be inadequately anesthetized or conscious during surgery.
- This problem led to the extensive investigation of the electroencephalogram (EEG) as a tool to monitor the CNS during anesthesia.
  - The EEG has a major advantage compared with techniques that measure changes in cardiovascular and respiratory variables, because it provides *direct* information about the functional integrity of the nervous system.

II. Monitoring the depth of anesthesia

- Anesthetists collate information based on clinical measurements and monitoring equipment to make an overall assessment of anesthetic depth.
  - A *single parameter* of anesthetic depth has yet to be described.
- The aim is to maintain the patient at an adequate depth of anesthesia for the surgical procedure without conscious awareness intraoperatively.

III. Methods of monitoring the depth of anesthesia

A. Evaluation of the eye

Position
- ○ The eye may rotate ventrally and medially during the early stages of anesthesia but returns to the center of the globe as anesthesia deepens.

Nystagmus
- ○ Lateral nystagmus is frequently observed during light anesthesia but disappears as anesthesia deepens.

Lacrimation
- ○ Common during light anesthesia; reduced or absent at a surgical plane of anesthesia.

Palpebral reflex
- ○ Elicited by gently stroking the eyelashes along the upper and lower eyelids.
- ○ The palpebral response is progressively depressed as anesthesia deepens. It is generally present, but slow and sluggish, at surgical planes of anesthesia.

Corneal reflex
- ○ Closure of the eyelids elicited by gentle pressure to the cornea.
- ○ The corneal reflex should be present during anesthesia: absence indicates excessive anesthetic-induced depression of the CNS.
- ○ *Touching the cornea carries the risk of corneal damage, and routinely eliciting a corneal reflex is not recommended.*
- ○ Repeated stimulation of the eye reflexes may result in reflex depression and reduced usefulness.

Effects of ketamine *or* tiletamine
- ○ Eye evaluation is of limited value following the administration of *ketamine* or *tiletamine* due to the following responses:
  - – Voluntary blinking.
  - – Lateral nystagmus.
  - – Central eye position.
  - – Lacrimation.

B. Movement

- ○ Movement indicates an inadequate plane of anesthesia.

C. Anal tone

- ○ Stimulation of the anus should cause reflex contraction of the anal sphincter.
- ○ This is an imprecise method to assess anesthetic depth, but may be useful when access to the patient's head is limited.
- ○ Absence of anal tone indicates too deep an anesthetic plane.

D. **Physiological parameters**

○ An increasing depth of anesthesia is commonly associated with reductions in heart and respiration rates, blood pressure, and cardiac output.

– However, these parameters are subject to multiple influences (particularly the effects of anesthetic drugs) during anesthesia, which limits their reliability as guides to depth of anesthesia.

– Additionally, heart rate tends to remain remarkably stable in horses.

○ Increases in arterial blood pressure indicate a decrease in anesthetic depth.

E. **Concentrations of inhalational anesthetic in expired gases**

○ End-tidal concentrations (expired) reflect brain concentrations following an equilibration period.

○ The dose of inhalational anesthetics administered is based on MAC.

○ A movement response to a noxious stimulus may occur at 1 MAC.

F. **Quantitative electroencephalography (EEG)** (see Section IV)

IV. EEG

● Electrical activity of the brain results from ionic currents generated by biochemical processes occurring at the cellular level.

● The principal generators of the EEG are thought to be dipole layers of *pyramidal neurones* in the cortical grey matter.

○ These cells are orientated in the same direction, so that summation of current flow originating from adjacent neurones occurs, generating electrical activity which can be recorded at the scalp surface.

● The potential for the EEG to be a measure of depth of anesthesia was recognized in the late 1930s.

● Fast Fourier Transformation (FFT) is now utilized to quantify information contained within the raw EEG signal and to facilitate interpretation of the data.

○ FFT transforms EEG data from the time to the frequency domain, producing a distribution of pure sine waves of varying frequencies which constitute the signal, described as a *power spectrum*.

○ A number of simple descriptors of the EEG signal can be derived from the power spectrum produced by FFT.

○ These include *median* and *spectral edge frequencies*, *total power* and power in the different frequency bands.

– *Median frequency*: frequency below which 50% of the total power of the EEG is located.

– *Spectral edge frequency* (95%): frequency below which 95% of the total power of the EEG is located.

– *Total power*: total area under the power spectrum curve.

– Changes in these variables have been used to assess depth of anesthesia.

A. EEG findings in the horse

- ○ EEG monitoring is not currently used in the clinical setting to measure depth of anesthesia.
- ○ However, a number of studies have investigated EEG changes during surgical stimulation.
  - – An increase in median frequency (demonstrating a shift towards high frequency activity) associated with the surgical stimulus of castration has been identified in *halothane*-anesthetized horses.
  - – Across species, there are discrepancies in the results of EEG studies of nociception, but this may be accounted for, in part, by a failure to use a standard surgical stimulus.
  - – EEG changes in *ponies* anesthetized with *halothane* in combination with different classes of intravenous drugs, found that only those with recognized antinociceptive efficacy reduced median frequency to a greater extent than spectral edge frequency 95%.
- ○ These studies suggest that changes in median frequency are associated with the antinociceptive efficacy of a drug. A good correlation has been demonstrated between EEG changes and drug concentration when each drug is administered as a single agent.
- ○ EEG changes associated with nociceptive stimulation have also been identified.
  - – However, when anesthesia is maintained with multiple drugs and the patient is subjected to intraoperative stimulation of varying intensity, robust EEG changes specifically associated with depth of anesthesia are less easy to identify.

EEG recording in the horse
- ○ Subcutaneous needle or self-adhesive silver chloride electrodes are used to record the equine EEG.
- ○ A three-electrode configuration is usually adopted.
  - – Reference electrode: parietal suture rostral to the divergence of the temporalis muscles.
  - – Active electrode: right zygomatic process.
  - – Ground electrode: caudal to the poll.

B. Auditory evoked potential (AEP)

- ○ The AEP is the response in the EEG to a *sound* stimulus.
- ○ It is extracted from the EEG by averaging the response to a number of stimuli so that the background noise of the underlying signal is eliminated.
- ○ The transient AEP consists of a series of positive and negative waves that represent the process of transmission and processing of auditory information from the cochlea to the brain stem, and the primary auditory and frontal cortex.
- ○ The waveform can be divided into *three parts*, depending on the latency of the appearance of the wave relative to the time of the auditory stimulus.
- ○ The use of middle latency (MLAEP) waves as an indicator of depth of anesthesia during EEG studies of intravenous drugs is of limited value.

C. Bispectral index (BIS)

- o BIS is a signal processing technique that decomposes the EEG signal to quantify the level of synchronization, in addition to amplitude and frequency variables, thus providing a more complex description of EEG pattern.
- o The output from the bispectral monitor is digital, making interpretation less complex than EEG data.
- o Studies in man have shown good correlation between adequacy of anesthesia and the BIS, although the finding is not universal.
  - – In an awake unpremedicated human being, BIS is typically > 90.
  - – A BIS < 60 is a strong indicator of unconsciousness.

BIS in the horse

- o BIS has been evaluated as an indicator of the degree of CNS depression in *isoflurane*-anesthetized horses.
  - – The BIS is significantly *less* in sedated and anesthetized horses compared with awake horses; however, BIS is *not* significantly different between sedated and anesthetized horses.
  - – This suggests that BIS may *not* be a useful technique for monitoring anesthetic depth during *isoflurane* anesthesia.
    - ■ The BIS is an index, empirically derived from human data.
- o Published studies investigating BIS in other animals are limited, but BIS has been found to be unreliable as a guide to CNS depression in *propofol* or *sevoflurane* anesthetized pigs.
- o The simplicity of BIS data interpretation makes an attractive clinical tool to measure anesthetic depth in animals; however, the derivation of the monitor from human data may make it less reliable for veterinary application.

Monitoring respiratory function

Deborah V. Wilson

- *General anesthesia* and *recumbency* in the horse are associated with very significant derangements in gas exchange and respiratory function. These changes may be life threatening for some horses.
- The *objective* when monitoring respiration is to ensure:
  - o Adequate oxygen content in the patient's arterial blood.
  - o Adequate removal of carbon dioxide.
- Monitoring respiratory function is an important part of maintaining homeostasis under anesthesia, and is the only way that respiratory dysfunction will be diagnosed.
- The American College of Veterinary Anesthesiologists has guidelines for monitoring respiration in horses under anesthesia that include the use of:
  - o Pulse oximetry.
  - o Capnometry.
  - o Arterial blood gas analysis.

- Other factors that help in the assessment of respiration include assessment of:
  - ○ Mucous membrane color.
  - ○ Thoracic wall and abdominal movement.
  - ○ Movement of the rebreathing bag.
  - ○ Tidal volume (spirometry).
- It is important to remember that monitors themselves require monitoring and calibration to ensure that they provide valid data.

I. Monitoring tidal volume and respiratory rate

A. Spontaneous ventilation

- ○ Observation of tidal volume (V_T) and respiratory rate (RR) constitutes the minimum in respiratory monitoring. However, this is an imprecise evaluation of respiratory function.
- ○ Low respiratory rates (< 5/min) are likely to result in hypoventilation (increased $PaCO_2$).
  - – Hypoventilation may cause hypoxemia.
- ○ However, higher respiratory rates and apparently adequate tidal volumes are no assurance that ventilation or oxygenation is adequate.

B. Controlled ventilation

- ○ A *respiratory rate* of 6–7/minute is usually suitable for adult horses.
  - – Higher rates (8–10/minute) can be used in foals.
- ○ The *tidal volume* required for a normal horse can be estimated as 10–15 ml/kg.
- ○ Peak *airway pressures* of 15–25 cmH$_2$O are usually associated with this tidal volume in normal, adult, full-sized horses.
  - – In conditions of reduced compliance (e.g. distended abdomen), much higher inspiratory pressures may be needed to deliver this tidal volume.
- ○ *Inspiratory time* is variable.
  - – In adult, full-sized horses, an inspiratory time of 2–3 seconds is necessary.
  - – In foals, an inspiratory time of 1–2 seconds is adequate.
  - – In cases of recurrent airway obstruction (RAO) or severe pulmonary atelectasis, a longer inspiratory time (up to 3 seconds) is recommended to facilitate recruitment of collapsed areas of lung.
  - – Increases in mean intrathoracic pressure occur as inspiratory time increases, which will then cause a decrease in cardiac output due to reduced venous return.

II. Monitoring carbon dioxide

- Arterial CO_2 ($PaCO_2$) is inversely related to alveolar ventilation (i.e. increases in alveolar ventilation decrease $PaCO_2$).

$$PaCO_2 \propto \frac{1}{V_A}$$

● Arterial CO_2 partial pressure can be measured:
  ○ Directly using blood gas analysis.
  ○ By estimation using end-tidal analysis.

End-tidal CO_2 analysis
  ○ The amount of CO_2 in the last part of the exhaled breath (end-tidal) is representative of that in alveolar gas, which closely matches $PaCO_2$.
  ○ End-tidal CO_2 partial pressures ($ETCO_2$) usually underestimate the $PaCO_2$.
    – The $PaCO_2$–$ETCO_2$ gradient in a normal, awake horse is 5–10 mmHg.
    – In foals, $ETCO_2$ is not a good predictor of $PaCO_2$ during spontaneous ventilation.
  ○ Increased dead space ventilation (areas of lung ventilated but not perfused) will cause an increase in the $PaCO_2$–$ETCO_2$ gradient.
    – The gradient is less variable when controlled ventilation is used, in comparison with spontaneous ventilation.
    – Gradients during *halothane* anesthesia can be up to 30 mmHg.
    – Gradient is greater in dorsal than lateral recumbency.
    – Gradient is expected to be greater in larger horses.

III. Types of carbon dioxide monitors (capnography)

A. Mainstream (non-diverting) gas analysers

  ○ In a mainstream (*non-diverting*) gas monitor the analysis occurs *inline*.
  ○ Used mainly for foals.

Advantages
  ○ Fast response.
  ○ No scavenging of sampled gases required.
  ○ Water and secretions are less of a problem.
  ○ Fewer disposable items used.

Disadvantages
  ○ Weight of the sensor.
  ○ Increased potential for leaks or disconnects in system.
  ○ Condensed water or secretions interfering with sensor.
  ○ Sensor is more vulnerable to damage.
  ○ Longer warm-up time.

B. Sidestream (diverting) gas analysers

  ○ Draws gas (using a pump) from the breathing system to the sensor which is located in the body of the monitor.
  ○ Sample gas is collected from a port in the Y-piece or a line placed within the endotracheal tube.
  ○ Used in adult horses.

Advantages
- o Faster warm-up.
- o Lightweight patient interface.
- o Several gases can be measured at once.
- o Monitor can be remote from patient (e.g. when using MRI).
- o Sampling from non-intubated patients is possible.

Disadvantages
- o Obstruction of tubing with water, blood, or secretions.
- o Delay in response dealing with sampled gas.
- o Needs calibration gas.

IV. Abnormal ETCO$_2$ values or waveform

A. Reasons for no ETCO$_2$ (or just a trace) on intubation

- o Esophageal intubation.
- o Apnea (squeeze rebreathing bag and ETCO$_2$ will register if tube in trachea).
- o Endotracheal tube blocked or kinked.
- o Obstruction of equipment or airway.

B. Reasons for increased ETCO$_2$

- o Hypoventilation.
- o Soda lime is ineffective leading to rebreathing of CO$_2$.
  - – The CO$_2$ tracing will be above zero during inspiration.
- o Anesthetic machine malfunction (e.g. one-way valves missing or stuck open).
- o Increased production of CO$_2$.
  - – Light plane of anesthesia with muscle activity (e.g. shivering, movement).
  - – Pathological states (e.g. malignant hyperthermia).
  - – Hyperthermia/pyrexia.
  - – Administration of bicarbonate (transient increase).

C. Decrease in ETCO$_2$

- o A *sudden* decrease in CO$_2$ needs to be investigated immediately.
- o Reasons for a decrease include:
  - – Circuit disconnection.
  - – Obstruction of endotracheal tube.
  - – Significant decrease in cardiac output (check blood pressure).
  - – Cardiac dysrhythmias (causing a reduced cardiac output).
  - – Cardiac arrest (delivery of CO$_2$ to the lungs requires blood flow).
  - – Pulmonary embolism.
  - – Monitor problem:
    - ■ Disconnection of sampling port.
    - ■ Obstruction of sampling line.
  - – Hyperventilation (gradual decrease).
  - – Hypothermia (gradual decrease).

D. Inspiratory ETCO$_2$ readings greater than zero

- o   Soda lime exhausted.
    - –   Should be accompanied by indicator turning purple.
- o   Expiratory valve malfunction (missing or stuck open).

E. Slow rate of rise or upstroke portion of waveform

- o   Obstruction of equipment or airway.
- o   Recurrent airway obstructive disease.

V. Sample capnograms (see Figs 14.1–14.4)
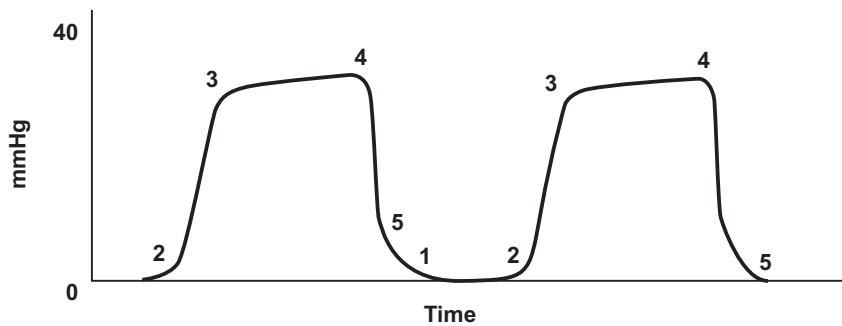
Fig. 14.1   A normal capnogram showing four separate phases. Phase 1–2 signifies the initial phase of expiration and the sampled gas is coming from anatomical dead space. The upstroke phase (2–3) indicates the presence of CO$_2$ in the sample. Point 4 signifies the highest value of expired CO$_2$ in phase 3–4 and is called the end-tidal CO$_2$ partial pressure. Phase 4–5 has a deep downstroke, and at point 4, CO$_2$-free gas is being inspired. The CO$_2$ partial pressure returns to zero, unless rebreathing is occurring.
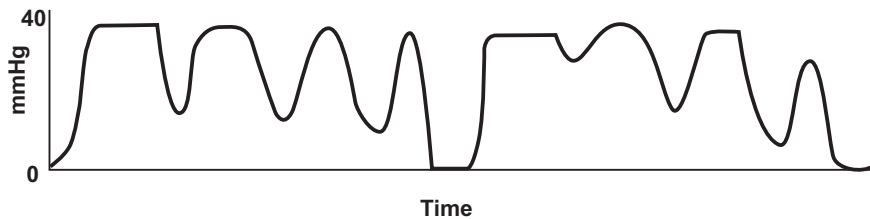
Fig. 14.2   'Fighting' the ventilator, with spontaneous ventilation intermingled with controlled ventilation.
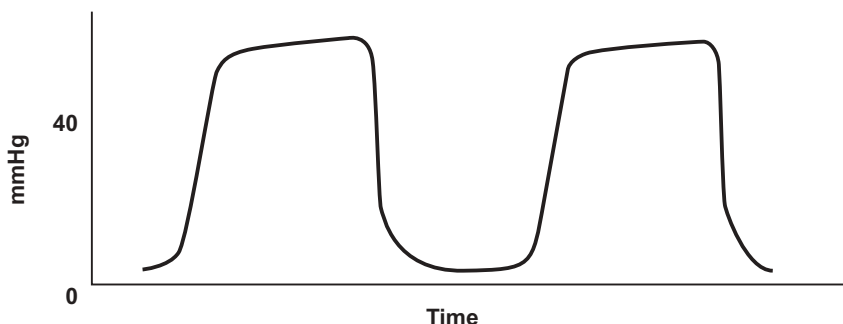
Fig. 14.3   Rebreathing of CO_2. The end-tidal partial pressure of CO_2 doesn't return to zero.
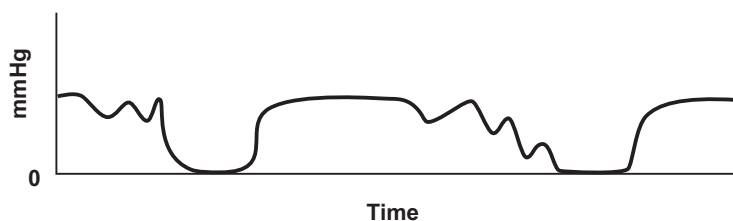
Fig. 14.4   Cardiogenic oscillations in the capnogram during controlled ventilation. Results from the heart beating against the lungs. Only likely to be observed in small foals on mechanical ventilation with low respiratory rates and a prolonged expiratory time. Oscillations are rhythmic and synchronized with heartbeat.

VI. Monitoring oxygen

- Inspired O_2.
  - The percentage of O_2 in the anesthetic circle is measured.
  - Monitoring inspired O_2 should guarantee that the horse is not receiving a hypoxic mixture.
  - This does not, however, guarantee that the oxygen *delivery* will be adequate, as this is a feature of lung and cardiovascular function.
- *Pulse oximetry* gives an indirect estimate of oxygenation (see Section VII).
- *Blood gas analysis* is the best method to evaluate respiratory function (see Section VIII).

VII. Pulse oximetry

- Allows the continuous calculation of O_2 saturation, using non-invasive technology.
- Measures hemoglobin (Hb) saturation and thus gives an indirect evaluation of PaO_2.
  - Hemoglobin saturation of 95–100% is normal.
    - Assuming normal functioning of the equipment, a saturation < 90% indicates the need for intervention.
  - The relationship between Hb saturation and PaO_2 is depicted by the oxyhemoglobin dissociation curve. (See Fig. 3.7.)

- Aids in detection of hypoxemia.
  - Hypoxemia is often undiagnosed and untreated in the horse.
  - Cyanosis is not always detectable in hypoxemic horses.

A. Technology

- Light-emitting diodes provide two sources of light which are passed through an arterial bed.
- The pulse oximeter compares absorption at the red (660 nm) and infrared (910 nm) wavelengths.
- Absorption of light of specific wavelengths relative to the ratio of oxyhemoglobin to deoxygenated (reduced) hemoglobin is transmitted to a photodetector to calculate O_2 saturation.
  – Oxygenated hemoglobin absorbs more infrared light and allows more red light to pass through.
  – Deoxygenated (reduced) hemoglobin absorbs more red light and allows more infrared light to pass through.
- The pulse oximeter with a plethysmographic trace also provides evidence of pulsatile blood flow at the probe site.

B. Factors affecting accuracy of pulse oximeter

- Abnormal readings will occur with probe site 'fatigue'.
- Movement artifact.
- Poor peripheral perfusion.
- Significant concentrations of carboxyhemoglobin and methemoglobin (saturation tends to be 85% regardless of oxygen saturation, SaO_2).

C. Probe placement

- Probe is usually placed on the tongue.
  – Alternate sites include the nostril, prepuce, vulva and lip.

D. Limitations of pulse oximetry

- Does not guarantee that sufficient O_2 is being delivered to tissues.
- Does not guarantee that tissues are utilizing O_2.
- Not always reliable in the horse.

VIII. Arterial blood gas analysis

- Blood gas analysis is the *gold standard* for assessment of acid–base status and respiratory function.
- Patient-side analyzers have made the method more available and affordable.
- The most common acid–base abnormalities encountered in anesthetized horses are:
  - Respiratory acidosis.
  - Metabolic alkalosis.
- *Venous* blood provides information about metabolic status, but not respiratory status.

A. Arterial oxygenation

- The PaO_2 is used to determine the efficiency of gas exchange in the lung.
- Normal values in horses breathing room air are 90–100 mmHg.
  - PaO_2 should increase if the horse is breathing an enriched O_2 mixture.
- In the standing horse, the alveolar–arterial O_2 gradient $[(A-a)\,PO_2]$ is ~ 10 mmHg.
- Therefore, the expected PaO_2 can be estimated from PAO_2 (calculated using the alveolar gas equation):

  Alveolar O_2 partial pressure $(PAO_2) = PIO_2 - PaCO_2/R$.
  $PIO_2 = $ Inspired O_2 fraction.
  R = respiratory gas exchange ratio (~ 0.8).
  $PaCO_2 = 40$ mmHg (35–45 mmHg).
  Water vapour pressure in airway is ~ 50 mmHg.
  Atmospheric air contains ~ 21% O_2.

  Example 1. An awake horse at sea level (atmospheric pressure is 760 mmHg).
  $PAO_2 = [21\%(760-50)] - 40/0.8$
  $PAO_2 = [0.21(760-50)] - 40/0.8$
  $\quad\quad = (0.21 \times 710) - 50$
  $\quad\quad = 149 - 50$
  $\quad\quad = 99$ mmHg

  PaO_2: So in this case, the expected PaO_2 would be ~ 90 mmHg.
- In horses under anesthesia, the PaO_2 is usually lower than expected.
  - Increases in $[(A-a)\,PO_2]$ may be due to:
    - V/Q mismatching.
    - Anatomical shunting.
    - Diffusion impairment.

  Example 2. An anesthetized horse at sea level (assuming $PaCO_2$ is 40 mmHg).
  Note: Assuming the horse is breathing 90% O_2, the PAO_2 should be much higher.
  $PAO_2 = [90\%(760-50)] - 40/0.8$
  $PAO_2 = [0.9(760-50)] - 40/0.8$
  $\quad\quad = (0.9 \times 710) - 50$
  $\quad\quad = 639 - 50$
  $\quad\quad = 589$ mmHg

  PaO_2: Based on the PAO_2, PaO_2 should be > 550 mmHg. However, in anesthetized horses, it is usually much lower, primarily due to V/Q mismatching.
- Factors causing hypoxemia, and their associated A – a gradients, are listed in Table 14.1.

Table 14.1   Causes of arterial hypoxemia and corresponding alveolar-arterial gradient.

Cause of hypoxemia	A-aDO$_2$
Hypoventilation	Normal
Diffusion abnormality	Normal
Ventilation/perfusion imbalance	Increased
Right-to-left shunt	Increased
Reduced inspired oxygen fraction	Normal

B. Arterial carbon dioxide partial pressures ($PaCO_2$)

o   Normal awake values are 35–45 mmHg.
o $PaCO_2$ is a direct measure of respiratory ventilation.
o   *Increased PaCO$_2$* is defined as *respiratory acidosis*. It is caused by:
   –   Hypoventilation.
      ■   Common in spontaneously breathing anesthetized horses.
   –   Hypermetabolic states (increased production of CO_2).
o   *Decreased PaCO$_2$* is defined as *respiratory alkalosis*. It is caused by
   –   Hyperventilation.
      ■   Only likely to occur during controlled ventilation.
   –   Hypothermia (resulting in decreased CO_2 production).
o   'Permissive hypercarbia' ($PaCO_2$ up to ~ 70 mmHg) is associated with higher cardiac output than normocarbia in anesthetized horses.
   –   Hypercarbia results in sympathetic stimulation.
o $PaCO_2$ increases by 4 mmHg/min during apnea in the anesthetized horse.
o   *Acute* changes in $PaCO_2$ cause changes in the pH.
   – $\uparrow PaCO_2$ by 20 mmHg = $\downarrow$ pH by ~0.08.
   – $\downarrow PaCO_2$ by 10 mmHg = $\uparrow$ pH by ~0.08.
o   Acute respiratory acidosis is uncompensated.
   –   The HCO_3 is usually < 30 mmHg.

Treatment of acute respiratory acidosis
●   The degree of hypercapnia which is acceptable during anesthesia of the horse is much debated, but it is generally agreed that controlled ventilation should be instituted at a $PaCO_2$ > 70 mmHg.

Monitoring cardiovascular function

Cardiovascular monitoring includes direct pulse palpation as well as more sophisticated methods such as direct arterial blood pressure and cardiac output measurements.

I. Evaluation of the arterial pulse by digital palpation

●   Simplest method of monitoring.
●   *Arteries used*: facial, transverse facial, metatarsal, digital and coccygeal.
●   Arterial pulse reflects peripheral perfusion.
●   Pulse strength is determined by the difference between systolic and diastolic pressure (pulse pressure difference) and also by vascular tone.
   o   Pulse pressure differences can be the same for different systolic and diastolic arterial pressures.
      Example: Systolic/diastolic readings of 120/80 and 80/40.
      –   Pulse pressure difference is 40 mmHg in both cases.
      –   When the pressure is 120/80, the pulse feels stronger because the higher vascular tone increases vessel turgor.
      –   For the second reading (80/40), the vessel wall is more readily collapsed with digital pressure.

II. Blood pressure

> Blood pressure (BP) = Cardiac output (CO) × Vascular resistance (VR).

● An indirect indicator of hemodynamic status.
  ○ Thus, changes in vascular resistance or blood volume affect blood pressure.

A. Indirect methods of measurement

Doppler method
  ○ Uses the return-to-flow principle and detects systolic pressure.
  ○ A cuff is placed around the tail, and the probe from the Doppler is placed over the coccygeal artery.
    – The width of the cuff should be 40% of the circumference of the tail.
    – Pressure is measured with an aneroid manometer.
  ○ The flow of blood through the vessels is detected by the probe and converted to an audible signal.
    – The cuff is inflated until the arterial flow ceases, and the audible signal stops.
    – The pressure in the cuff is slowly released, and the reading on the aneroid mano-meter at which the audible signal is heard again corresponds to systolic blood pressure.
    – Diastolic pressure is identified as a change in tone.
  ○ *Disadvantages*:
    – Erroneous readings result if probe is not placed properly.
    – False readings result from incorrect cuff size.
    – Difficulty in locating signal if pressures are low.
    – Diastolic pressure is not always accurately determined.
    – Impractical when access to the tail is limited.

Oscillometric method
  ○ Detects changes in the intracuff pressure (caused by the pulse wave) from which systolic, diastolic, mean pressure, and heart rate are calculated.
    – The width of the cuff should be 40% of the circumference of the limb/tail.
  ○ More reliable in the foal than the adult horse.
  ○ *Disadvantages*:
    – Many units are designed to detect heart rates > 30–40, which limits their useful-ness in adult horses.
    – False readings result from incorrect cuff size.

B. Direct methods of measurement

  ○ The preferred method of blood pressure measurement.
  ○ Requires catheterization of a peripheral artery (20- or 22-gauge catheter).
  ○ Arteries used include: metatarsal, facial, transverse facial, coccygeal.

- ○ The catheter can be connected to a transducer and amplifier to display continuous readouts of systolic, diastolic, mean blood pressure, and pulse waveform on an oscilloscope.
    - – Alternatively, the catheter can be connected to an aneroid manometer using a liquid/air interface, for *mean* blood pressure measurement.
- ○ The transducer or the liquid/air interface of the aneroid manometer needs to be zeroed at the *level of the heart* for accurate readings.
- ○ *Disadvantages*:
    - – It is subject to errors including:
        - ■ Improper zeroing of transducer.
        - ■ Excessively long tubing between catheter and transducer.
        - ■ Walls of tubing not sufficiently rigid.
        - ■ Air bubbles in the system.
    - – Arterial catherization may not always be possible for technical reasons.
    - – Complications resulting from catheterization (e.g. hematoma, infection).

III. Cardiac output determination

- ● Cardiac output is a better indicator of hemodynamic status than is blood pressure.
- ● Not commonly measured because of its complexity and invasiveness.
- ● Cardiac output (liters/min) = Heart rate × Stroke volume.
                                = Blood pressure/Vascular resistance.

A. Thermodilution method

- ○ Is more commonly employed in the research than the clinical setting.
- ○ Requires a special, multiport catheter (Swan-Ganz) which is advanced into the pulmonary artery via a jugular vein, and an injection of a solution of known temperature into the right atrium.
- ○ The temperature change in the pulmonary artery, caused by mixing of the injectate with the blood, is detected by a thermistor at the distal end of the catheter.
- ○ Cardiac output is estimated from the area under the temperature–time curve.
- ○ *Disadvantages*:
    - – Catheter placement requires expertise.
    - – Increased morbidity due to infection, dysrhythmias and pulmonary artery rupture from catheterization.
    - – Cost of equipment.

B. Lithium dilution method

- ○ A less invasive method than thermodilution.
    - – No need for cardiac catheterization.
- ○ Requires injection of *lithium chloride* into a peripheral or central vein and catheterization of a peripheral artery.
    - – A sensor attached to the arterial catheter detects the concentration change of lithium caused by its dilution in the blood.
- ○ This method correlates closely with the thermodilution method.

o   More practical than thermodilution method in the clinical setting.
o   *Disadvantage*:
  –   Cost of equipment.

C. Partial carbon dioxide rebreathing method

o   Non-invasive.
o   End-tidal CO_2 and hemoglobin saturation are required to derive cardiac output.
o   Uses a rebreathing loop which is attached to the Y-piece of the circuit, which forces a partial, temporary rebreathing of CO_2.
o   Differences in CO_2 elimination and end-tidal CO_2 between the normal and the rebreathing state are used to compute cardiac output using an alternate form of the Fick equation.
o   Upper limit measurement is 20 liters/min.
o CO_2 elimination restricts patient size to ~ 20–100 kg.
o   Suitable for use in the clinical setting.
o   *Disadvantages*:
  –   Cost of equipment.
  –   Can only be performed in the anesthetized horse (foal).
  –   More reliable in ventilated patients.
  –   Loop size limited to small anesthetic circuits.
  –   Not suitable for adult, full-sized horses.

D. Echocardiographic method

o   Minimally invasive.
o   Includes transthoracic techniques using Doppler or volumetric methods.
o   Very useful in the clinical setting.
o   *Disadvantages*:
  –   Cost of equipment.
  –   Equipment requires software for calculation of hemodynamic parameters.
  –   Position of the animal may alter results.

Anesthetic agent monitoring

Deborah V. Wilson

A. Reasons to monitor

o   The expired concentration of an inhalational anesthetic gives a good approximation of its concentration in the brain, provided a period of equilibration is allowed.
  –   Equilibration takes longer with more soluble anesthetics (e.g. *halothane*).
o   Allows a more precise and scientific approach to delivering anesthetics.
o   It is virtually impossible to estimate the inspired and expired concentrations of anesthetic in horses, especially if relatively low fresh gas flows are used.
o   When adjunctive drugs are used, monitoring allows the minimum concentration of inhalational anesthetic to be used.

B. Interference by methane

- o Fermentation processes in the equine large intestine produce a large volume of methane.
- o Horses excrete some of this methane via the lungs, and it can accumulate in the anesthetic circuit especially if low fresh gas flows are employed.
- o Infrared (IR) absorption or mass spectroscopy are utilized to measure inhaled and exhaled anesthetic.
- o Some IR analyzers read methane as an inhalational anesthetic and thus give very high concentration readings (> 6%). This is obviously not a desirable feature of a monitor for equine use.
  - – Methane absorbs IR light at a wavelength of 3.3 μm.
  - – Anesthetic agent analyzers that function around 3.3 μm are subject to large errors.
  - – Monitors that function within the range 10–13 μm are not affected by expired methane.

Monitoring neuromuscular blockade

Elizabeth A. Martinez

It is important that neuromuscular blockade be monitored during anesthesia. The horse should be observed closely during the recovery period for signs of unexpected residual paralysis attributable to organ function compromise or drug interactions.

I. Evaluating neuromuscular blockade

A. Benefits of monitoring

- o Allows for accurate dosing and the detection of residual paralysis.
  - – Residual paralysis during the recovery period can lead to muscle weakness and respiratory depression.
  - – Difficulty in standing because of muscle weakness can lead to serious injury either to the horse or to personnel.

B. Evoked responses

- o Visual observation of evoked responses is the most common method in clinical practice.
  - – Involves supramaximal stimulation of a peripheral nerve and observation of the strength of the evoked response before and after administration of the relaxant.

C. Stimulation sites

- o The *facial* and *superficial peroneal* nerves are the most commonly used sites.
- o Contact electrodes are placed on either side of the nerve and attached to a handheld peripheral nerve stimulator.

○ The response following stimulation at these two sites is not identical.
○ The facial muscles are more resistant to the effects of muscle relaxants than are the extensor muscles of the hind limb.
○ After administration of a muscle relaxant, the facial twitch may weaken, but *fade* may or may not be present, even if all hoof twitches have disappeared.
  – This difference may be important when deciding whether to administer additional muscle relaxant and in determining if residual paralysis exists.

D. Train-of-four

○ The train-of-four (TOF) pattern of nerve stimulation is often used to assess the depth of neuromuscular blockade.
○ The TOF consists of four supramaximal impulses delivered at 2 Hz (2 twitches/second).
○ The degree of blockade is evaluated by comparing the strength of the fourth twitch with that of the first.
  – Prior to administration of the muscle relaxant, the ratio is 1.0.
  – The twitch ratio decreases as the depth of neuromuscular blockade increases.
  – As the block deepens, the twitches disappear. The fourth twitch disappears first, followed by the third, second, and lastly the first twitch.
  – During recovery, the twitches return in reverse order.
  – A twitch ratio ≥ 0.7 corresponds to clinical signs of adequate recovery.

E. Tetanic stimulation

○ Is sometimes useful in detecting residual paralysis when the TOF response is back to baseline strength.
○ Tetanic stimulation involves delivering serial supramaximal stimulation at a high frequency (50 Hz) for 5 seconds.
○ In the non-paralyzed horse, a tetanic stimulus results in sustained muscle contraction.
○ If residual paralysis is present, 'fade' of the evoked response will occur due to the inability to maintain the strength of contraction.
○ Since tetanic stimulation can be painful, the horse must be adequately anesthetized before the stimulus is delivered.

II. Antagonism of neuromuscular blockade

A. Succinylcholine and mivacurium

○ Recovery from either is due to rapid hydrolysis by plasma cholinesterase.
○ Recovery may be prolonged if plasma cholinesterase activity is decreased.

B. Nondepolarizing muscle relaxants

○ May be antagonized with the administration of an anticholinesterase drug.
  – The most commonly used anticholinesterase drugs in veterinary medicine are *pyridostigmine*, *neostigmine*, and *edrophonium*.

C. Anticholinesterase drugs

- o Act by inhibiting the enzyme acetylcholinesterase, which is responsible for the hydrolysis of ACh.
  - – When an anticholinesterase drug is given, ACh accumulates at nicotinic and muscarinic receptor sites.
  - – Since nondepolarizing muscle relaxants act by competing with ACh for the same receptor binding sites, the resultant increase in ACh tips the balance in favor of ACh and neuromuscular transmission is restored.
- o *Adverse effects*:
  - – Include undesirable muscarinic effects (e.g. bradycardia, hypotension, salivation, diarrhea).
  - – An anticholinergic drug (e.g. *atropine*) may be administered prior to antagonism to prevent or attenuate these side effects.
    - ■ However, anticholinergic drugs can cause unwanted gastrointestinal effects (e.g. colic and/or ileus).

Edrophonium
- o The muscarinic effects of *edrophonium* are mild compared with those of either *pyridostigmine* or *neostigmine*. Therefore, it may be administered to a horse *without* prior or concomitant anticholinergic therapy.
- o The dose of *edrophonium* in the horse is 0.5–1.0 mg/kg, IV.
- o It should be given slowly, over approximately 60 seconds.
- o The horse should be observed for changes in *heart rate* or arterial *blood pressure*.

D. Reversing a deep blockade

- o It is recommended that signs of spontaneous recovery be present prior to antagonism with an anticholinesterase drug.
- o If a deep blockade is present, higher doses of the reversal agent are required, increasing the likelihood of unwanted side effects.

15 Management of sedation and anesthesia

Standing sedation

Surgical and diagnostic procedures are often performed in standing horses. In instances where general anesthesia may be contraindicated due to risk factors (e.g. on an HYPP horse), standing sedation may be indicated. The most commonly used drugs are α_2 agonists, which may be used alone or in combination with other drugs (e.g. opioids or phenothiazines).

I. Advantages of standing sedation over general anesthesia

- Lower risk of anesthetic-related complications.
  - Reduced morbidity/mortality.
  - Less cardiorespiratory depression.
  - Reduced risk associated with induction and recovery.
- Reduced cost.
- Reduced time to complete the procedure (in most cases).

II. Disadvantages of standing sedation

- Oversedation can result in excessive ataxia.
- Insufficient analgesia may be a problem.
- Less than ideal surgical conditions (e.g. movement).
- Increased injury risk to personnel.

III. Properties of an ideal sedative drug

- Reliable sedation.
- Reversible.
- Predictable onset and duration of action.
- Minimal ataxia.
- Analgesia.
- Minimal cardiorespiratory effects.
- Can be used in combination with other sedatives/tranquillizers.
- Small injectate volume.
- No allergic reactions.

IV. Drug regimens used for sedation

● Sedation may be maintained either with *bolus* injections or as *constant infusions*.

A. Bolus injections

○ A bolus injection of drugs is the most common mode of administration.
○ Effects occur rapidly after IV administration and may result in oversedation.
○ Therefore, use of lower doses initially and assessment of effects is preferred.

Alpha$_2$ agonists (IV doses)
○ *Detomidine*: 5–20 µg/kg (0.005–0.02 mg/kg).
○ *Xylazine*: 0.3–1.0 mg/kg.
○ *Medetomidine*: 3.5–7 µg/kg (0.0035–0.007 mg/kg).
○ *Romifidine*: 30–100 µg/kg (0.03–0.1 mg/kg).

Alpha$_2$ agonists in combination with opioids
○ Sedation with an α_2 agonist should precede the opioid administration.
○ This combination is generally used for surgical procedures requiring a higher degree of sedation and analgesia.
○ Individual drug doses may need to be adjusted to obtain the desired effect.

Examples (IV doses)
■ *Xylazine* (0.5–1 mg/kg) + *butorphanol* (0.02–0.05 mg/kg).
■ *Medetomidine* (0.0035–0.005 mg/kg) + *methadone* (0.1 mg/kg).
■ *Detomidine* (0.005–0.01 mg/kg) + *morphine* (0.15 mg/kg).
■ *Xylazine* (0.5–1 mg/kg) + *morphine* (0.15 mg/kg).
■ *Detomidine* (0.005–0.01 mg/kg) + *butorphanol* (0.02–0.05 mg/kg).
■ *Romifidine* (0.05–0.1 mg/kg) + *butorphanol* (0.02–0.05 mg/kg).

Alpha$_2$ agonists in combination with phenothiazines
○ Ideally, the phenothiazine should be administered before (15–30 min) the α_2 agonist.
 – Due to the slow onset of effect.
○ The analgesia is less intense than with the opioid combination.

Examples (IV doses)
■ *Acepromazine* (0.02–0.05 mg/kg) + *xylazine* (0.5–1 mg/kg).
■ *Acepromazine* (0.02–0.05 mg/kg) + *detomidine* (0.005–0.01 mg/kg).

B. Constant rate infusions (CRI)

○ CRI provides a more constant state of sedation once the loading bolus has been administered.
 – If a loading bolus is not administered, it requires 4–5 times the half-life of the drug to achieve therapeutic concentrations.
○ Administration of a CRI requires an IV catheter and accurate infusion settings.

Examples

■ *Medetomidine* bolus: 0.005 mg/kg; CRI: 0.0035 mg/kg/h.

> *To administer to a 450 kg horse*:
> Add 2 mg *medetomidine* to 500 ml saline (4 μg/ml).
> Infuse 1 drop/s (if using a 10 drops/ml set).
> Solution will last 80 min.

■ *Detomidine* bolus: 0.008 mg/kg; CRI: 0.04 mg/kg/h.

> *To administer to a 450 kg horse*:
> Add 25 mg to 500 ml saline (50 μg/ml).
> Infuse 1 drop/s (if using a 10 drops/ml set).
> Solution will last 80 min.

■ *Butorphanol* bolus: 0.02 mg/kg; CRI: 0.024 mg/kg/h.

> *To administer to a 450 kg horse*:
> Add 15 mg to 500 ml saline (30 μg/ml).
> Infuse 1 drop/s (if using a 10 drops/ml set).
> Solution will last 80 min.

○ When using combinations, individual CRI doses should be halved to avoid oversedation.

Example

■ *Medetomidine + Butorphanol*:
Medetomidine bolus: 0.005 mg/kg; CRI 0.018 mg/kg/h.
Butorphanol bolus: 0.02 mg/kg; CRI at 0.012 mg/kg/h.

> *To administer to a 450 kg horse*.
> Add 7.5 mg of *butorphanol* and 1 mg of *medetomidine* to 500 ml saline (15 μg/ml *butorphanol* and 2 μg/ml *medetomidine*).
> Infuse 1 drop/s (if using a 10 drops/ml set).
> Solution will last 80 min.

General anesthesia techniques

General anesthesia involves an *induction phase*, which is generally achieved with injectable drugs, and a *maintenance phase*, which may be achieved with either injectable drugs or inhalational anesthetics or a combination of the two.

I. Induction of anesthesia

● Induction of anesthesia should include the use of a sedative drug prior to administration of the induction drug.
   ○ In some cases (e.g. α_2 agonists), the sedative will also have analgesic properties.

A. Reasons to sedate prior to induction

○ To facilitate handling.
○ To smoothe induction.
○ To decrease dose of induction drug(s).

- o To decrease dose of maintenance drug(s)
  - – e.g. decrease MAC of inhalational anesthetics.
- o To improve analgesia (e.g. α_2 agonists, opioids).
- o To improve recovery.

Drugs used for sedation
- o Alpha$_2$ agonists alone or with opioids or phenothiazines.
- o Phenothiazines alone or with opioids or α_2 agonists.

B. Drugs commonly used for induction

- o *Ketamine.*
- o *Ketamine* and a benzodiazepine.
- o *Thiopental.*
- o *Tiletamine/zolazepam.*
- o Inhalational anesthetics (e.g. in foals).

C. Examples of induction regimens

Ketamine (2.0–2.5 mg/kg, IV) following an α_2 agonist
- o *Xylazine* (1.0–1.5 mg/kg, IV).
  - – Short duration (5–10 min of surgical anesthesia).
  - – Shorter lasting than regimens 3–4 below.
- o *Detomidine* (0.01–0.02 mg/kg, IV).
  - – Longer duration than *xylazine*.
- o *Romifidine* (0.08–0.12 mg/kg, IV).
  - – Longer duration than *xylazine*.
- o *Medetomidine* (0.005–0075 mg/kg, IV).

Ketamine (2.0–2.5 mg/kg, IV) + benzodiazepine, following α_2 agonist
- o *Diazepam/midazolam* (0.02–0.1 mg/kg, IV) improves relaxation.
- o Alpha$_2$ agonist dose may be reduced, if so desired.

Ketamine (2.0–2.5 mg/kg, IV) + guaiphenesin, following α_2 agonist
- o *Guaiphenesin* (50–100 mg/kg, IV).
- o Improves relaxation.
- o Alpha$_2$ agonist dose may be reduced, if so desired.

Tiletamine/zolazepam (1–2 mg/kg, IV) following α_2 agonist
- o Longer duration (10–20 min depending on dose) than *ketamine* (5–10 min).
- o Good relaxation (*zolazepam*).
- o Recovery not as good as with α_2/ketamine, but acceptable.
  - – Recovery is better with lower dose rates.

Thiopental (3–5 mg/kg, IV) following α_2 agonists
- o Use full dose of the α_2 agonist.
- o Good relaxation.
- o Analgesia only from the α_2 agonist.

Thiopental (3–5 mg/kg, IV) + guaiphenesin following α_2 *agonist*
- o   Can be mixed with *guaiphenesin* (50–100 mg/kg) and infused together.
- o   Lower dose of the α_2 agonist may be used, if so desired.
- o   Good relaxation.
- o   Analgesia only from the α_2 agonist.

Propofol (2 mg/kg, IV) following α_2 *agonist*
- o   Use full dose of the α_2 agonist.
- o   Myoclonus and paddling may occur.
- o   Some horses become excited.
- o   Short duration of surgical anesthesia.

Inhalational anesthetics with or without sedation
- o   *Isoflurane* or *sevoflurane* are preferred over *halothane*.
- o   Has been recommended for foals.
    - –   But has been associated with increased mortality compared with injectable induction.

II. Prolonging anesthesia with injectable drugs (see TIVA)

- ●   Prolongation of general anesthesia, beyond the effect of the induction drugs, is frequently necessary.

A. Short-term prolongation using intermittent bolus injection

- o   **Alpha$_2$ agonist/ketamine** (one-quarter to one-half of induction dose of each).
    - –   Extends anesthesia by 5–10 min.
- o   **Thiopental** (1–2 mg/kg. This is one-quarter to one-half of the induction dose (3–5 mg/kg)).
    - –   Extends anesthesia by 5–10 min.
    - –   Not a good choice if *thiopental* is used as the sole induction drug.

B. Long-term prolongation using constant rate injection

- o   Maintains a more stable plane of anesthesia.
- o   *Ketamine*, *xylazine*, and *guaiphenesin* are the most common combination.

Example: Infusion for a 450 kg horse
- o   **Ketamine** (1–2 g) + **xylazine** (500 mg) in 1 liter of **guaiphenesin** (5%).
    - –   Infused at a rate of 2–3 ml/kg/h.

III. Prolonging anesthesia with inhalational anesthetics
(see next section, Inhalational anesthesia)

- ●   Inhalational anesthetics are generally used to maintain anesthesia following induction with injectable drugs.

IV. Prolonging anesthesia with a combination of inhalational and intravenous anesthetics (see PIVA)

Inhalational anesthesia

- Inhalational anesthetics are commonly used to maintain general anesthesia.
- They have also been recommended for *induction* of anesthesia in foals.
- Inhalational anesthetics have a narrow therapeutic index (LD_{50}/ED_{50}) compared with injectable anesthetics.

I. Clinical use of inhalational anesthetics

A. As the sole anesthetic

○ Although feasible in foals, inhalational anesthetics have been associated with a higher mortality than injectable drugs, especially when used as the sole agents for induction and maintenance of anesthesia.

B. Maintenance of anesthesia

○ Most common reason for administering inhalational anesthetics.
  – Induction is usually achieved with injectable drugs.

C. Maintenance of anesthesia in association with injectable drugs

○ Inhalational anesthetics may be used in conjunction with injectable drugs.
○ Injectable drugs reduce the MAC of the volatile anesthetic and provide analgesia. (See PIVA.)

II. Potential advantages of inhalational anesthetics

- Anesthetic depth can be changed rapidly (with modern drugs).
- Drug concentrations can be monitored with end-tidal monitors.
- Minimal drug accumulation over time (with modern drugs).
- Elimination is ventilation dependent.

III. Potential disadvantages of inhalational anesthetics

- Pollution of surgical suite.
- Cardiorespiratory depression.
- Minimal analgesia.
- Equipment is expensive as are modern inhalational drugs.

- Narrow therapeutic index.
- Recovery from anesthesia is not as good as with intravenous drugs.

IV. Recovery

A. Recovery quality

- Negatively correlated with the duration of anesthesia.
- For anesthetic periods of *less than 2 hours*, *halothane* results in more controlled, although longer, recoveries than *isoflurane*.
- For anesthetic periods of *more than 3 hours*, *isoflurane* results in better recoveries than *halothane*.
- *Sevoflurane* causes less ataxia than *isoflurane* during recovery.

B. Improving recovery

- Use of sedatives or tranquilizers, including the α_2 agonists and *acepromazine*, is recommended in the recovery period to prevent the horse from attempting to stand before the 'hang-over' effect of the inhalational anesthetic is eliminated.

V. Mortality and general anesthesia

- Equine mortality rate from anesthetic-related causes is estimated at 1 death per 1250 for elective procedures.
  - Mortality rate has been similar among the different inhalational anesthetics except in horses 2–5 years of age, where *isoflurane* decreases death rate fivefold over *halothane*.
  - *Isoflurane*, *sevoflurane*, and *desflurane* are better options for the critically ill horse.

Total intravenous anesthesia (TIVA)

I. Historical perspective

- TIVA has its roots in the anesthetic triad (*narcosis–analgesia–relaxation*) that was proposed for anesthesia of human patients in the 1950s. These effects are achieved by utilizing a 'balanced' anesthesia technique in which two or more drugs are combined to produce the desired effects.
- Prior to the introduction of volatile anesthetics in the 1960s, intravenous drugs were widely used for general anesthesia of horses.
  - *Chloral hydrate*, alone or in combination with *pentobarbital sodium* or *magnesium sulphate*, was the intravenous technique most commonly employed.
- A renewed interest in TIVA has been facilitated by the development of newer, safer compounds, and recognition of an unacceptably high mortality and morbidity rate with inhalational anesthesia.

II. Potential advantages of TIVA over inhalational anesthetics

- Less cardiorespiratory depression.
- Superior analgesia.
- Morbidity and mortality may be lower.
- Less likelihood of movement in response to surgical stimuli.
- Improved recoveries.
- Decreased surgical stress.
- Minimum organ toxicity.
- No pollution of surgical suite.

III. Potential disadvantages of TIVA

- Drug accumulation and a build-up of active metabolites with prolonged infusions.
  - This can be managed by decreasing the infusion rate over time.
- A fluid or syringe pump is necessary for accurate drug delivery.

IV. Methods of drug delivery

- Under ideal circumstances the amount of drug delivered, per unit time, should equal the drug's clearance (C_L).
- A constant rate infusion (CRI) should maintain a steady-state plasma concentration (Cp).
- A constant rate infusion is based on C_L and Cp and can be expressed, in its simplest form as:
  $$\text{CRI (µg/kg/min)} = \text{Cp (µg/ml)} \times C_L \text{ (ml/min/kg)}.$$

A. Intermittent injection of drugs

- Is the simplest method of drug delivery.
- It is satisfactory for maintaining anesthesia of short duration.
- However, it is not possible to maintain a steady plasma concentration using this method.

B. Drip technique

- Drugs are added to commercial bags of isotonic fluids.
  - Commercial fluid bags are overfilled, so this is a source of error.
- Drip chamber is adjusted to give the desired flow rate.
- For large volumes of injectate, it may be necessary to withdraw an equal volume of crystalloid from the fluid bag before adding the drug(s).

C. Infusion pump

- Can be programmed to deliver a specific volume of fluid in a given time.
- The drugs to be infused are added to commercial bags of replacement fluids (e.g. 0.9% NaCl).
- This method is more accurate than the drip technique.

D. **Syringe pump**

- Is an accurate method for delivering smaller volumes.

E. **Computerized syringe pump**

- A more sophisticated method of delivery.
- Pump delivers 'target-controlled infusions' based on drug-specific, kinetic/dynamic data incorporated into specific software programs.
- *These systems have not been developed for any drug in the horse*.

V. Choice of injectable drugs

- No one drug can adequately supply the basic components of balanced anesthesia (sleep, relaxation, analgesia).
  - Therefore, two or more drugs are used in TIVA.
- The *context-sensitive half-life* (CSHL) is an important concept to consider when infusing anesthetic drugs.
  - The CSHL is the time for the plasma concentration (Cp) to decrease by 50% following a specified time of infusion.
- For all drugs, the CSHL increases with infusion time.
  - The CSHL is relatively short for *propofol* and long for *thiopental*.
    - Therefore, prolonged infusions of *thiopental* result in long recoveries.

VI. Properties of an ideal injectable anesthetic

A. **Physicochemical properties**

- Water-soluble.
- No preservatives.
- Long shelf life.
- Stable on exposure to heat and light.
- Small volume.
- Compatible with other drugs.

B. **Pharmacodynamic properties**

- Wide therapeutic index (LD_{50}/ED_{50}).
- Rapid onset of action.
- Short duration.
- Analgesic.
- Metabolites non-toxic and inactive.
- Rapid recovery with no hangover effect.

C. No side effects

- o   No histamine release.
- o   No cardiorespiratory depression.
- o   No gastrointestinal effects (e.g. ileus).
- o   No allergic reactions.
- o   No local toxicity (non-irritant to tissues).

VII. Drug combinations used in TIVA

- •   Older regimens included *chloral hydrate*, either alone or in combination with *pentobarbital* and *magnesium sulphate*.
  - o   Rarely used nowadays.
- •   Modern regimens use drugs with kinetic profiles more suited to infusions.

A. Ketamine + alpha$_2$ agonist

- o   Are the most widely studied TIVA combinations.
- o   Anesthesia is induced with *ketamine* (or *ketamine/benzodiazepine*) following sedation with the α_2 agonist.
- o   Anesthesia is maintained with intermittent boluses or, preferably, an infusion.
- o   *Ketamine* and an α_2 agonist provide poor relaxation and for that reason *guaiphenesin* is often added.

B. Ketamine + xylazine + guaiphenesin

- o   *Ketamine* (2 g) + *xylazine* (500 mg) in 1 liter of *guaiphenesin* (5%).
- o   Infused at a rate of 2–3 ml/kg/h.

C. Ketamine + detomidine + guaiphenesin

- o   *Ketamine* (2 g) + *detomidine* (20 mg) in 1 liter of *guaiphenesin* (5%).
- o   Infused at a rate of 1–2 ml/kg/h.

D. Ketamine + romifidine + guaiphenesin

- o   *Ketamine* (2 g) + *romifidine* (50 mg) in 1 liter of *guaiphenesin* (5%).
- o   Infused at a rate of 2–3 ml/kg/h.

E. Ketamine + medetomidine

- o   *Ketamine* (2 g) + *medetomidine* (2.5 mg) in 1 liter of *guaiphenesin* (5%).
- o   Infused at a rate of 2–3 ml/kg/h.

F. Ketamine + benzodiazepines

- o   *Ketamine* (6 mg/kg/h) + *climazolam* (0.04 mg/kg/h).

   o   Ataxia may be a concern following prolonged infusions of climazolam.
       – *Climazolam* can be reversed [*flumazenil* (0.04 mg/kg, IV) or *sarmazenil* (0.04 mg/kg, IV)] 20 min following cessation of *ketamine*. (Waiting 20 min gives time for the plasma *ketamine* concentration to decrease.)

G. Propofol

   o   Has the most suitable kinetic profile for TIVA.
   o   Has a short duration of action and is rapidly cleared.
   o   However, if used alone for TIVA it has the following disadvantages:
       – Hypotension.
       – Respiratory depression.
       – Poor analgesia.
       – Poor inductions.
   o   In an attempt to improve the quality of anesthesia, *propofol* has been combined with a number of drugs, thereby allowing for a reduced dose of *propofol*. The following are examples:

Propofol (0.14 mg/kg/min) + ketamine (0.05 mg/kg/min)
   o   Following induction with *detomidine* (0.02 mg/kg) and *ketamine* (2.2 mg/kg).
   o   Reduces the cardiorespiratory depression of *propofol* and enhances analgesia.

Propofol (2 mg/kg for induction and 0.2 mg/kg/min)
   o   Following *detomidine* (0.015 mg/kg) sedation.
       – Inductions are poor in some cases despite sedation.

Propofol (0.09 mg/kg/min) and medetomidine (0.0035 mg/kg/h)
   o   Following induction with *medetomidine* (7 µg/kg) and *ketamine* (2.2 mg/kg).

VIII. Influence of premedication on TIVA

●   It is important to consider the effects of premedication (e.g. *acepromazine*) when calculating TIVA dosages, as premedication may allow lower doses of drugs to be used for maintenance.

Partial intravenous anesthesia (PIVA)

●   PIVA is the combined use of *inhalational* and *intravenous* anesthetics to produce the desired degree of general anesthesia.
●   The goal of PIVA, as for TIVA, is to achieve a state of 'balanced' anesthesia by using two or more drugs in combination.
●   By reducing the delivered concentration of inhalational anesthetics, their negative cardiorespiratory effects will be reduced; provided they are replaced by intravenous drugs with less depressant effects.

I. Potential advantages of PIVA

- Reduced cardiorespiratory depression (lower concentration of inhalational drugs).
- Superior analgesia.
- Decreased organ toxicity.
- Decreased pollution of surgical suite.
- Decreased likelihood of intraoperative movement in response to surgical stimulus.
- Improved outcome (i.e. better recoveries, decreased morbidity and mortality).
- Benefits of muscle-relaxing effects of inhalational anesthetic.
- Minimal accumulation of inhalational anesthetic (using modern drugs) over time.

II. Potential disadvantages of PIVA

- Potential for pollution, although reduced, exists.
- Cardiovascular depression of inhalational drugs, although reduced, is present.
- Need to have equipment to deliver IV and inhalational drugs.
- Intravenous drug accumulation will occur during long procedures unless their dose rate is decreased over time.

III. Choice of intravenous drugs for PIVA

- Since the major goals of PIVA are to (1) provide analgesia, (2) reduce MAC, and (3) reduce inhalational anesthetic-associated cardiovascular depression, drugs chosen for PIVA should, at least, meet these requirements. Desirable traits include:
  - MAC reduction (e.g. *ketamine*, α_2 agonists, *lidocaine*).
  - Analgesia (e.g. *ketamine*, α_2 agonists, *lidocaine*).
  - Minimum effects on cardiovascular system (e.g. *ketamine*, *lidocaine*).
  - Minimal organ toxicity at clinical doses (e.g. *ketamine*, *lidocaine*, α_2 agonists).
  - Short context-sensitive half-life (e.g. *propofol*).
  - Reduction of stress response (e.g. α_2 agonists).
  - Compatible with other drugs used for infusion.

Comment: As in the case of TIVA, no one drug can meet all these requirements; therefore, more than one intravenous drug is often used with inhalational anesthesia.

IV. Examples of drugs and drug regimens use in PIVA

- A variety of injectable drugs and drug combinations can be used in PIVA.

A. Ketamine
  - Reduces MAC by ~ 30% @ 3 mg/kg/h.

B. Alpha$_2$ agonists

- o *Medetomidine* (0.0035–0.005 mg/kg/h).
  - – Expected MAC reduction ~25%.
- o *Xylazine* (1 mg/kg/h).
  - – Expected MAC reduction ~ 25%.

C. Ketamine and alpha$_2$ agonists

- o Can be mixed together and infused.
- o Expected MAC reduction at aforementioned doses is ~ 50–60%.
  - – MAC reduction is dose-dependent and additive.

D. Lidocaine

- o Dose-dependent MAC reduction.
  - – MAC reduction @ 3 mg/kg/h ~ 25%.
  - – MAC reduction @ 6 mg/kg/h ~ 50%.

E. Lidocaine (4 mg/kg/h) + ketamine (3 mg/kg/h)

- o Combination reduces MAC by 60–80%.
- o Can be mixed together for infusion.

F. Lidocaine (4 mg/kg/h) + ketamine (3 mg/kg/h) + xylazine (1 mg/kg/h)

- o MAC reduction of 80–90%.
- o Can be mixed together for infusion.

G. Lidocaine (4 mg/kg/h) + ketamine (3 mg/kg/h) + medetomidine (0.0035 mg/kg/h)

- o MAC reduction of 80–90%.
- o Can be mixed together for infusion.

H. Propofol

- o Can be used in PIVA but has disadvantages.
  - – Does not provide analgesia.
  - – Is cardiorespiratory depressant.
- o Combining with other intravenous agents (e.g. *ketamine*) reduces the dose of *propofol* needed and dose-related adverse effects.

Comment: Injectable drugs accumulate over time, so it may be prudent to decrease the doses during prolonged procedures.

	Anesthesia of foals

- The normal full-term foal is well developed at birth but is in a transition phase to adult circulatory and pulmonary systems and, thus, is physiologically fragile.
- Pulmonary changes occur during the first few hours but the most important changes to the adult circulatory system take 48–72 hours.

I. Transition to adult life

A. Fetal circulation

- o Has three major shunts (placental, foramen ovale, ductus arteriosus) and blood is delivered from the dam via the umbilical vein.
    - – The fetal foal does *not* have a ductus venosus.
- o Initial expansion of the lungs requires a high negative intrathoracic pressure and is followed by a dramatic decrease in pulmonary vascular resistance.
- o *Expansion of the lungs results in*:
    - – Increased pulmonary blood flow.
    - – Closure of foramen ovale.
    - – Closure of the ductus arteriosus (constriction of spiral smooth muscle) results from:
        - ■ Increased PaO_2.
        - ■ Decrease in prostaglandins.

B. Reopening of shunts

- o Initial closing of fetal vascular shunts is not anatomically complete, and permanent closure takes 2–4 weeks (longer if the foal is *premature*).
- o *Shunts can reopen in response to*:
    - – Hypoxemia.
        - ■ Decreased constrictor response to PaO_2 in neonate.
        - ■ Shunts are more likely to remain open (or reopen) in a *premature foal*.
    - – Hypercarbia.
    - – Acidemia.

II. Respiratory system of the neonatal foal

A. Breathing pattern

- o Increased respiratory rate.
- o Increased airflow rate.
- o Increased minute ventilation (liters/kg).
- o Lung and chest wall compliance is greater than that of an adult.

B. **Control of breathing**

o   Neural and chemical control similar to those of adult.
   –   Neural system is probably immature at birth.
o   Differences in magnitude of response to changes in PaO_2 and $PaCO_2$.

C. **High alveolar ventilation rate in foal is due to:**

o   Increased oxygen consumption/kg (6–8 ml/kg/min).
   –   Due to increased sympathetic activity because of increased *work of breathing*.
o   An attempt to minimize energy expenditure.
   –   Elastic work is minimized with rapid, shallow breathing.

D. **Arterial blood gas values in neonatal foals**

o   Foals are capable of establishing adequate pulmonary ventilation within a few minutes of birth and the major changes in ventilation occur in the first hour of life.
o PaO_2 values are low (~ 40 mmHg) immediately following birth but increase (~ 60 mmHg) at 1 h, and by 4 h are up to 75 mmHg. However, adult values are not achieved for about 7 days.
   –   Hypoxemia has been attributed to a *right to left shunt* which may be intrapulmonary or intracardiac in origin.
   –   It is important to consider the effect of *lateral recumbency* on PaO_2 values.
      ■ PaO_2 values in lateral recumbancy are 10–15 mmHg less than those in the standing foal.
o $PaCO_2$ values are ~ 50 mmHg in the first hour of life and decrease thereafter.

Supplemental O_2
o   Breathing O_2 via a mask for 2–3 min will significantly increase PaO_2.
   –   Therefore, O_2 should be supplied in this fashion at induction of anesthesia.

III. Cardiovascular system of the foal

●   Higher cardiac index (ml/kg/min) than the adult.
   o   Achieved primarily by an increase in heart rate.
●   Ventricular compliance is limited.
●   Sympathetic system and baroreceptors are immature.

IV. Thermoregulation

●   To maintain body temperature, the foal must be able to produce heat.

A. **Heat production occurs by:**

o   Voluntary muscle activity.
   –   Will be inadequate in a sick foal or during anesthesia.

- ○ Involuntary muscle activity (generation of heat through increased muscle tone).
  - – Poorly developed in neonate.
- ○ Non-shivering thermogenesis (brown fat) is vital to neonate.
  - – Inhibited by surgery and sympathetic blockade.

B. Heat loss is exacerbated by:

- ○ Foal's small body mass.
- ○ Low body fat content.
- ○ High surface area to body mass ratio.

C. Neutral thermal environment

- ○ Is the range of ambient temperatures within which body temperature can be maintained at minimum O_2 expenditure.
- ○ Foals are especially prone to heat imbalances.
  - – Range of neutral thermal temperatures is narrow for neonates.
  - – These temperatures are higher than those for an adult.

D. Importance of heat conservation

- ○ The increased metabolic rate required to increase body temperature can result in:
  - – Hypoxemia (from increased O_2 consumption).
  - – Hypoglycemia.

E. Effects of anesthesia on heat balance

- ○ Heat transfer from core to periphery is facilitated by:
  - – Decreased vasomotor tone resulting in vasodilation.
  - – Increased skin blood flow (e.g. barbiturates).
  - – Impairment of central control mechanisms.
    - ■ Vasoconstriction not triggered until core temperature is low.

F. Effects of hypothermia on anesthesia

- ○ Decreased minimum alveolar concentation (MAC).
- ○ Decreased tissue perfusion resulting in delayed drug elimination.
- ○ Decreased metabolism.
- ○ Increased bleeding (decreased clotting function).
- ○ Delayed recovery.
- ○ Increased O_2 consumption (e.g. from shivering in recovery).

V. Drug metabolism and excretion

- ● It appears that the mechanisms responsible for drug metabolism and excretion are relatively well developed in the neonatal foal.

- Metabolic function develops *in utero*.
  - ○ Even though the placenta is primarily responsible for metabolic homeostasis, the fetal kidney has a role in regulating amniotic fluid volume.
  - ○ The foal kidney has adequate ability to deal with sodium and water loads indicating a good ability to excrete drugs.
- Hepatic enzyme activity is probably adequate for all enzymatic systems.

VI. Anesthesia

A. Preoperative evaluation

- ○ It is especially important in the neonatal foal to determine if there are congenital cardiac defects which may increase the anesthetic risk.
- ○ Determination of *colostrum* intake is important, and a plasma transfusion should be considered if the IgG concentration is low (<800 mg/dl).
- ○ Blood glucose should be evaluated, as hypoglycemia can develop if the foal is not sucking or is bacteremic.

B. Fasting

- ○ In general, the *neonatal foal* should be allowed to suck up to the time of anesthesia induction; however,
  - – If the foal is being tube fed it may be necessary to withhold milk for a period as many of these sick foals have delayed gastric emptying.
- ○ *Older foals*, on solid food, may have food withheld from 4–6 hours.
  - – It is unclear whether this is beneficial.

C. Sedation

- ○ Young foals usually become recumbent when sedated.
  - – This can facilitate the performance of non-painful procedures such as radiographs.
- ○ To prevent *hypothermia* and *hypoglycemia*, avoid keeping the neonatal foal sedated for long periods and choose a technique that will allow a fast return to normal activity.
- ○ It is also advisable to provide O_2 via a mask while the foal is sedated.

Benzodiazepines
- ○ *Diazepam/midazolam* 0.05–0.1 mg/kg, IV, can be used for sedation of neonatal foals.
  - – Ataxia will develop, so the standing foal must be supported after drug administration until it becomes recumbent.
  - – Large doses or repeated dosing will produce prolonged ataxia.

Alpha$_2$ agonists
- ○ Use with caution (low doses to effect) in the very young.
- ○ Avoid in the sick neonatal foal.
- ○ Older foals may be sedated with an α_2 agonist, as follows, with the higher end of the dose range being used for older and stronger foals.

Xylazine: 0.3–1.0 mg/kg, IV.
Detomidine: 0.005–0.01 mg/kg, IV.
Medetomidine: 0.0035–0.005 mg/kg, IV.
Romifidine: 0.03–0.1 mg/kg, IV.

Anticholinergic drugs
- o Rarely indicated.

D. Drug doses for neonatal foals

Injectable drugs
- o Neonatal foals may require lower doses of injectable anesthetic agents than adults. This may be due to:
  - – A greater proportion of cardiac output going to the *vessel-rich group* (heart and brain).
  - – Immature central nervous system.
  - – Increased sensitivity of receptors.
  - – More permeable blood–brain barrier.
- o Decreased plasma protein binding.
- o The effects of the aforementioned factors may be offset by:
  - – Increased total body water and extracellular fluid.

Inhalational anesthetics
- o Neonatal foals would be expected to have a lower MAC for inhalational anesthetics, but this has not been studied extensively.
- o Proposed reasons for a reduced MAC in the neonate include:
  - – Immature central nervous system.
  - – Decreased pain sensitivity.
  - – Progesterone.
  - – Increased endorphin concentrations.

E. Drug doses for older foals

- o Older foals will generally require higher doses of injectable and inhalational anesthetics than adults or neonates.
  - – This may be partly a result of their excitable nature and an increased extracellular fluid volume compared with adults.
- o MAC increases with age until adulthood and then declines.

F. Induction of anesthesia with an inhalational anesthetic

- o Has been recommended for foals, especially for neonates.
- o Can be done following minimal or no sedation.
- o The anesthetic can be delivered via a circle system using either a facemask or following nasotracheal intubation.
- o While this method of induction is often advocated for sick foals, it must be understood that inhalational anesthetics have, in general, a lower therapeutic index than injectable agents.

o   Inhalational anesthetic induction has been associated with an *increase in mortality*.
  –   This higher mortality rate may be a consequence of the relatively rapid uptake of volatile agents in neonates.

Reasons for rapid uptake of volatile anesthetics in neonate
  o   High alveolar ventilation (liters/minute) relative to functional residual capacity.
  o   Lower anesthetic solubility in blood.
    –   Due to differences in plasma constituents (e.g. albumin, triglycerides).
  o   Lower anesthetic solubility in tissues.
    –   Due to a higher water content and decreased protein and lipid concentration.
  o   Cardiac output is preferentially distributed to *vessel-rich group* (e.g. brain/heart).

G. Induction of anesthesia with an intravenous drug(s)

  o   Choice of drug(s) is generally based on the experience and personal preference of the anesthetist.
  o   Regardless of drug choice, it is advisable to administer the drug(s) *slowly*.
    –   This will prevent overdosing (which may result in apnea).
    –   Slow administration will allow the opportunity for O_2 to be provided, via a mask, during the induction process.

Light plane of anesthesia
  o   Neonatal foals may be kept in a 'light' plane of anesthesia for minimally invasive, brief procedures (e.g. joint lavage) using a mixture of *ketamine* and a benzodiazepine.
  o   *Ketamine* (1.0–2.0 mg/kg, IV) can be mixed with *diazepam* (0.05 mg/kg) and dosed to effect to induce recumbency and to maintain the desired degree of anesthesia.
  o   For older foals, *ketamine* can be mixed with an α_2 agonist and dosed to effect.
    –   Alternatively, the foal could be premedicated with *xylazine* (0.5–1.0 mg/kg; IV) and induced with a benzodiazepine/*ketamine* mixture, to effect.

Deep plane of anesthesia
  o   *Ketamine* (2–3 mg/kg, IV) with *diazepam*/*midazolam* given slowly to effect ± a low-dose α_2 agonist (depending on physical status and age).
  o   *Propofol* (2 mg/kg, IV) given slowly to effect with or without prior sedation with a benzodiazepine.
    –   More likely to induce apnea than *ketamine* and has minimal analgesia.

H. Maintenance of anesthesia

  o   As in the case of induction agents, the choice of maintenance drugs is based on experience and personal preference.
  o   The merits of maintenance with inhalational anesthetics, TIVA, and PIVA are discussed in the relevant sections.
    –   Foals do *not* have prolonged recovery following PIVA with *ketamine*, low-dose *lidocaine* and *isoflurane*.

VII. Monitoring and patient care

A. Positioning and padding

- As with all anesthetized patients, attention should be given to proper positioning and padding.
- The relatively long limbs of the foal need to be supported, and bony prominences should be protected.

B. Monitoring

- Ideally, should include:

Cardiovascular
- It appears that the anesthetized foal can have a lower blood pressure than that which is acceptable in the adult and still have adequate cardiac output.
  – A lower mean blood pressure (40–60 mmHg) appears to be acceptable in the neonate.
  – Cardiac output is heart-rate dependent in foals; therefore, bradycardia (<50 beats/min) is generally unacceptable.

Ventilation
- Should be controlled, as hypoventilation is common in neonates regardless of type of anesthesia.
  – Maintain $PaCO_2 < 50–60$ mmHg.
  – Ensure an adequate PaO_2.

Body temperature
- May decrease even if *active heating* is provided.
- Attempts should be made to keep heat losses to a minimum.
  – Ideally, it is best to position the heating blanket (e.g. circulating warm water or forced air) on top of the foal rather than underneath, since closure of surface blood vessels is likely to be induced by the pressure of the foal's body mass.
  – However, this may not be practical if the foal is in dorsal recumbency. Also, it carries the risk of the heating blanket being damaged by towel clamps.

Blood glucose
- May decrease during long surgeries, especially in sick neonates.
  – Monitoring blood glucose is particularly important in these cases.
  – A helpful guide is to administer dextrose (5%) in lactated Ringer's at 3–5 ml/kg/h to maintain normoglycemia.
- Routine administration of dextrose, in the absence of monitoring, may result in hyperglycemia in some instances. This may result in hyperinsulinemia and rebound hypoglycemia if the foal does not have an energy source (e.g. milk or further IV dextrose) soon after recovery.
- Sick foals on total parenteral nutrition (TPN) should have their blood glucose closely monitored if the TPN is discontinued in the perioperative period.

VIII. Recoveries

- Foals should be kept warm in recovery.
- Assisted recovery is recommended for neonates.

IX. Anesthesia for uroperitoneum

- Rupture of the urinary bladder is a condition which requires prompt surgical correction, and affected foals generally have significant cardiovascular and metabolic derangements.
- This condition occurs mainly in colt foals (<1%) and is believed to result from the increase in intra-abdominal pressure when passing through the pelvic canal.

A. Clinical presentation

- o Usually presents within the first 3 days of life.
- o Signs include:
  - – Depression and loss of interest in sucking.
  - – Dehydration.
  - – Straining to pass urine.
    - ■ The volume of urine passed will depend on the size of the defect in the bladder and its anatomical location.
  - – Abdominal distension.
    - ■ Occurs over time and causes pain and compromise of lung function.
- o The severities of clinical and metabolic changes are dependent on the age of the foal and whether any urine can be voided.

B. Metabolic changes

- o The main changes are a decrease in plasma Na^+ and Cl^- and an increase in K^+.

Hyponatremia (<125 mEq/liter)
- o Is the result of an increase in extracellular fluid due to abdominal distension with urine.
- o Results in depression, muscle weakness and anorexia.
- o Central nervous system changes are rare, probably because the change in plasma $[Na^+]$ occurs slowly.

Hyperkalemia (>5.5 mEq/liter)
- o Results from the inability to excrete potassium in the urine.
- o Signs of hyperkalemia are $[K^+]$ dependent and mainly involve the cardiovascular and neuromuscular (muscle weakness) systems.
- o ECG changes include:
  - – Dysrhythmias (e.g. heart block).
  - – Tall T waves (occur at plasma $[K^+] \geq 5.5$ mEq/liter).
  - – Widened QRS (usually indicates that plasma $[K^+] \geq 6.5$ mEq/liter).
  - – Atrial systole (no P wave indicates that plasma $[K^+] \geq 6.5$ mEq/liter).
  - – Prolonged P–R interval (indicates that plasma $[K^+] \geq 6.5$ mEq/liter).

C. **Preoperative treatment**

- o   It is important to decrease plasma $[K^+]$ to <6 mEq/liter and improve circulating volume before proceeding with anesthesia.
- o   Although it is technically possible to drain the abdomen of urine, it is very time consuming and is poorly tolerated by the foal.
- o   Administration of large volumes of isotonic intravenous fluids will further dilute the plasma Na^+ and distend the abdomen.
- o   IV *potassium penicillin* may increase $[K^+]$ and should be used with caution.

Plasma volume expansion
- o   Hypertonic saline (5 ml/kg) will increase intravascular volume and increase plasma $[Na^+]$ by approximately 8 mEq/liter.
  - –   The aim is to increase the $[Na^+]$ to the value at which neurological signs are allayed rather than return $[Na^+]$ to normal.
  - –   Also, increasing plasma $[Na^+]$ may counteract the effects of hyperkalemia on cardiac arrhythmias.
- o   Potassium-free replacement fluids (e.g. 0.9% NaCl) are recommended during surgery; however, standard replacement fluids containing K (e.g. lactated Ringer's, Normosol R) are acceptable because they expand circulating volume and have a low $[K^+]$ (thus do not increase plasma $[K^+]$).

Reduce plasma $[K^+]$
- o   Expand intravascular volume (as with hypertonic saline).
- o   Transfer potassium into cells:
  - –   *Dextrose* infusion will increase insulin release; however, the onset of its effect is slow, and it is *not reliable* in reducing plasma $[K^+]$.
  - –   *Insulin* (0.1–0.2 IU/kg, regular insulin, IV) in 5% *dextrose* (3–5 ml/kg). This will reduce the potassium to <5.5 mEq/liter by the end of the 30-min infusion.
  - –   *Correct metabolic acidosis*. (A decrease in pH causes an increase in plasma $[K^+]$.)
    - ■   However, significant metabolic acidosis is not a common finding.
  - –   *Sodium bicarbonate* may not be effective in lowering plasma $[K^+]$ in foals that are not acidemic.
    - ■   Administration of $NaHCO_3$ does not appear to protect against hyperkalemia-induced arrhythmias.
    - ■   It may also result in a reduction in plasma ionized calcium which would be especially detrimental in this situation.

Reverse membrane effects of hyperkalemia
- o   To reduce the arrhythmogenic effects of hyperkalemia, the following are recommended:
  - –   *Beta$_1$ agonists* (e.g. *dobutamine*) may be efficacious in heart block and the effect is relatively rapid. *This treatment is recommended in an emergency*.
  - –   *Calcium chloride* (1 ml/10 kg of a 10% solution) infused slowly. It is not very effective in emergency situations.
  - –   Increasing plasma $[Na^+]$, as with hypertonic saline, seems to have a protective effect.

D. Anesthesia

- ○ Avoid agents with dysrhythmogenic potential (e.g. α_2 agonists).
- ○ Induce with a mixture of a benzodiazepine (*diazepam*/*midazolam*) and *ketamine*. The mixture should be given slowly to effect.
- ○ Give O_2 during induction.
- ○ Anesthesia may be maintained with inhalational anesthetics.
  - – *Isoflurane* and *sevoflurane* are better choices than *halothane*.
- ○ To reduce the chances of dysrhythmias occurring, a lower concentration of inhalational anesthetics can be delivered.
  - – An infusion of *ketamine* (3 mg/kg/h) should reduce MAC by at least 30%.
  - – It is important to remember that the neonatal foal will have a lower MAC.
- ○ Ventilation should be controlled, as hypoventilation is likely to occur due to the effects of anesthetic drugs and the increased intra-abdominal pressure.

E. Monitoring

- ○ In addition to routine monitoring, plasma *glucose* and *potassium* should be checked periodically.

Anesthesia of horses with intestinal emergencies (colic)

- The overall risk of mortality in anesthesia of intestinal colic cases is about 10 times that of elective cases.
  - ○ The increased risk is probably multifactorial, but cardiovascular compromise and endotoxemia are important contributors.
- Horses anesthetized for abdominal problems vary greatly in physiological status.
  - ○ Those with chronic intermittent colic are usually physiologically stable, as are horses in the early stages of acute large colon displacement.
  - ○ Horses with advanced small intestinal obstruction and those with large colon torsion can be *in extremis* at presentation.

I. Preoperative evaluation

- Horses may be in a state of cardiovascular compromise due to a shift of fluids and electrolytes into the distended small intestine.
  - ○ This results in a decrease in intravascular volume and reduced preload and cardiac output.
- Change in cardiovascular function is reflected in high heart rates, weak peripheral pulses, increased capillary refill times, and pale or cyanotic mucous membranes.
- Pain, resulting from intestinal distension and stretching of mesentery, may make the horse uncontrollable without medication.
- Abdominal distension (e.g. from large bowel torsion) can compromise respiratory and cardiovascular function.

- Gastric distension, if unrelieved:
  - May result in aspiration (from reflux of gastric contents into the pharynx).
  - May lead to gastric rupture.
- Passage of a *stomach tube* is part of the initial evaluation process, and the tube is usually kept in place during anesthesia.

II. Preparation for anesthesia

- Once the decision to perform surgery is reached, the horse usually needs to be treated rapidly and this generally includes:

A. Fluid therapy

  - In most cases the intravascular volume will be reduced significantly.

Isotonic fluids (e.g. lactated Ringer's, Normosol R)
  - Large volumes (40–60 ml/kg) are needed (20–30 liters for a dehydrated 500 kg horse).
    - This takes a relatively long time to administer.
    - This contributes to interstitial edema.
  - Isotonic fluids don't remain in the circulation long, especially in shock states.

Hypertonic saline
  - An effective alternative to isotonic fluids.
  - Solutions of ~ 7% NaCl appear to be most efficacious.
  - Small volumes are effective (4–5 ml/kg of 7.2% NaCl).
  - Can be administered rapidly (5–10 min).
  - Increases intravascular volume due to osmotic effect.
  - Positive inotropic action.
  - Cardiovascular effects last ~ 45–60 min.
  - Anti-inflammatory effect (decreased prostaglandin formation).
  - Inexpensive.

Colloids
  - Are solutions containing large molecules (e.g. Hetastarch, dextrans) which exert an oncotic effect and thereby expand the intravascular volume.
  - Relatively small volumes (5–10 ml/kg) are efficacious.
  - Hetastarch has the ability to 'plug' leaks in endothelium.
  - Decrease formation of adhesion molecules by LPS-stimulated endothelium.
  - Longer dwell time in vascular space.
  - Decrease volume of isotonic crystalloid needed for resuscitation.

Comment: In adult horses (500 kg), *hypertonic saline* (~ 7%) is the most practical treatment. A volume of 2 liters (4 ml/kg) is sufficient and causes significant improvement in cardiac output. For a more prolonged effect, hypertonic saline can be combined with Hetastarch (5–10 ml/kg).

Acid–base correction
- o   Is generally unnecessary, as few of these cases have significant metabolic acidosis.
- o   Intravascular volume status should be improved before attempting treatment with $NaHCO_3$.

B. Sedation and analgesia

- o   May be necessary in order to control a painful horse prior to anesthesia.

Alpha$_2$ agonists
- o   Provide sedation and analgesia.
- o   Low doses (e.g. *xylazine*, 0.3 mg/kg, IV) may be given as needed.
- o   *Detomidine* may have a more negative effect on gastrointestinal motility.

NSAIDs
- o   Examples include *flunixin*, *phenylbutazone*, and *ketoprofen.*
- o   Used for analgesia and anti-inflammatory effects in endotoxemic horses.

Opioids
- o   May be given IV with an α_2 agonist or given alone IM.
- o   The onset of action is not as rapid as α_2 agonists, and large doses can cause excitement.
  - –   *Morphine* (0.15 mg/kg IV; 0.25 mg/kg IM) is an effective analgesic.
  - –   *Butorphanol* (0.02–0.05 mg/kg, IV; 0.1 mg/kg, IM) is less efficacious than *morphine* but seems to be associated with a favorable outcome when given as a constant-rate infusion in the postoperative period.
  - –   *Methadone* (0.05–0.1 mg/kg) and *meperidine* (1–2 mg/kg, IM) are used more commonly in European countries than in the USA.

Phenothiazines
- o   Generally contraindicated in colic patients due to their vasodilating actions which have a negative effect on preload in the volume-depleted horse.

C. Anti-endotoxin therapy

- o   A high percentage of horses are either endotoxemic at presentation or become so as surgery progresses.

Polymixin B
- o   Has a high affinity for the lipid A component of LPS.
- o   Its effects in endotoxemic horses are dose-dependent.
  - –   Dose: 1000–6000 IU/kg, IV.
- o   It has the potential to cause *nephrotoxicity*, but that does not appear to be a problem with short-term use at the recommended doses.

Anti-endotoxin serum
- o   Does not appear to be as efficacious as polymixin B and may cause adverse reactions.

D. NSAIDs

- ○ Efficacious at decreasing prostaglandin formation in response to LPS administration.

E. Dimethylsulphoxide

- ○ Efficacious in endotoxic shock models and is sometimes used in colic cases.
    - – Decreases TNFα production.

F. Antimicrobial therapy

- ○ Usually consists of a β lactam (e.g. *K penicillin*) and an aminoglycoside (e.g. *gentamicin*).
- ○ Since dramatic decreases in blood pressure can follow the administration of *K penicillin* to the anesthetized horse, it should be given (slowly) prior to induction.
    - – Otherwise, administer very slowly (~15 min) during anesthesia.
- ○ It may be beneficial to administer anti-endotoxin therapy prior to antimicrobials.
    - – Administration of β lactam antimicrobials causes an increase in the plasma concentration of LPS due to their actions on the bacterial cell wall.

III. Sedation and induction

- If the horse has had sedatives and analgesics in the evaluation phase, further sedation may not be required (depending on the method of induction).
- In horses with poor circulatory status, the onset of drug effect may be prolonged.
- The choice of induction regimens is a matter of personal preference and may include one of the following (see 'General anesthesia techniques', p. 208, for doses):
    - ○ Alpha$_2$ agonist + *ketamine*.
    - ○ Alpha$_2$ agonist + *ketamine* + *diazepam/midazolam*.
        - – Benzodiazepines allow a lower dose of α$_2$ agonist and improve relaxation.
    - ○ Alpha$_2$ agonist + *tiletamine/zolazepam*.
        - – Longer acting than *ketamine*.
        - – Smooth transition to the inhalational anesthetic.
        - – Cause a significant, time-dependent reduction in the concentration of inhalational anesthetic needed in the first hour following induction.
    - ○ *Guaiphenesin* (~50 mg/kg) + *ketamine* (2 mg/kg) or *guaiphenesin* (~50 mg/kg) + *thiopental* (3 mg/kg) following sedation with an α$_2$ agonist.

IV. Intubation and oxygenation

- Sternal recumbency is recommended for intubation if gastric reflux is likely.
    - ○ Aspiration is a risk, particularly in acute colic cases.
- Oxygen supplementation and positive pressure ventilation are particularly important if the abdomen is distended (e.g. large colon torsion).
    - ○ A *demand valve* is an effective way to deliver O$_2$ immediately following induction.

- Controlled ventilation is recommended throughout the anesthetic period.
  - With severe abdominal distension, relatively high airway pressures will be required to ventilate the lungs.
  - The goal of ventilation is to improve O_2 delivery rather than to reduce end-tidal CO_2 to normal.
    - It may not be possible to achieve an end-tidal CO_2 in the normal range until the abdomen is opened, without the use of excessive airway pressures.
    - High intrathoracic pressures impede venous return and cardiac output.

V. Maintenance of anesthesia

- Endotoxemic horses anesthetized for colic surgery often appear to need lower doses of maintenance anesthetics.
  - This may be a direct result of endotoxemia as LPS administration to laboratory rodents causes a significant decrease in MAC.
- The potential advantages of TIVA or PIVA are worth considering.

VI. Intraoperative support

A. Fluid therapy

Isotonic fluids
  - Are a suitable choice.
  - Examples: lactated Ringer's, Normosol R.
  - Infusion rates of 10–20 ml/kg/h may be required.

Colloids
  - Indicated if hypoproteinemia is present.
    - A dose of 5–10 ml/kg may be necessary, and this can be infused slowly in association with isotonic fluids.
    - Colloids will also decrease the volume of isotonic fluid needed.
  - Example: Hetastarch.

B. Cardiovascular support
  - Consists of improving preload and providing inotropic support.

Preload
  - Is improved by fluid replacement.

Inotropic support
  - Is best achieved with a cardioselective β_1 adrenergic agonist.
  - Endotoxemic horses seem to require higher doses of β_1 agonists to maintain an acceptable blood pressure.
  - Beta$_1$ agonists enhance Ca^{++} entry into the sarcolemma of cardiac myocytes.
    - *Dobutamine* (~ 0.5–5 µg/kg/min) is a cardioselective β_1 agonist.

– *Dopamine* (~ 0.5–5 µg/kg/min) is not cardioselective.
– *Ephedrine* (0.05–0.1 mg/kg, as a slow bolus) is not as effective as *dobutamine* and, because it crosses the blood–brain barrier, may increase the MAC of inhalational anesthetics. It also has a greater potential to cause arrhythmias.

Comment: Some severely endotoxemic horses remain hypotensive despite heroic attempts at resuscitation with fluids and inotropes. However, most of these horses seem to have a good outcome in the short term, despite the hypotension, and rarely develop complications such as myopathy. In such cases, it may be best to tolerate a lower mean blood pressure to avoid β_1 agonist-induced tachycardia (>70 beats/min), which may further reduce preload.

Calcium infusions
o Most sick colic cases have low plasma ionized calcium, despite total calcium being normal.
o Calcium should be infused IV *slowly*, and up to 20 mg/kg can be given over the course of the surgery.
o Calcium will also provide *inotropic* support.
o Commercial preparations for large animals generally contain ~10 g of calcium and variable amounts of dextrose and magnesium (<3 g).

VII. Recovery

● In most cases, horses recover slowly and quietly following colic surgery.
● Many of these horses have become exhausted prior to surgery and seem content to rest.
   o It is best to allow the horse time to recover, and myopathy does not seem to be a concern in long recoveries if the horse is recovered on a *padded* surface.
● The stomach tube should be removed as the end of surgery approaches. Generally, gastric reflux will have ceased by then.
   o It should be removed slowly and carefully to prevent nasal bleeding.
● The urinary bladder will probably have filled during surgery and should be catheterized and emptied in male horses.
   o A full bladder will make the horse uncomfortable and may provoke early attempts to stand.
   o This is less important in mares as their bladders often empty spontaneously during surgery and recovery.
● The airway needs to be protected from aspiration of gastric contents.
   o The head can be tilted downwards to facilitate pharyngeal drainage.
   o Due to the head-down position during surgery, nasal edema will be present; if the orotracheal tube is removed, a patent nasal passage must be established.

VIII. Intraoperatative use of phenylephrine

● When *nephrosplenic entrapment* of intestine is present, *phenylephrine* may be used intra-operatively to contract the spleen and facilitate correction of the problem.
● Low doses of *phenylephrine* (0.01 mg/kg, IV/5 min) may be effective.
   o It is prudent to start with low doses to avoid causing extreme hypertension.

Anesthesia of donkeys and mules

Although donkeys and mules do not differ greatly from horses as regards the management of anesthesia, they have some anatomical, physiological and behavioral differences which need to be considered.

I. Behavioral differences

- Most domestic donkeys have a resigned nature but mules can be difficult to handle.

II. Anatomical differences

A. Airway
- When compared with similar sized horses, donkeys and mules have narrower nasal passages, larynx, and trachea.
    - These differences are reflected in the need for a slightly smaller endotracheal tube relative to a horse of similar weight.

B. Jugular catheterization
- Somewhat more difficult due to the presence of thicker skin over the jugular furrow.

III. Differences in drug dosages

- Differences in metabolism and responses to anesthetics and analgesics have been documented between donkeys and horses, and among breeds of donkeys.
    - For many anesthetic drugs, the difference in response between donkeys and horses may reflect differences in receptor density in the CNS rather than differences in drug disposition.
- In general, *donkeys eliminate drugs faster* than do horses, and this would indicate more frequent dosing for a specific blood concentration to be maintained.
- Generally, for anesthetic drugs, donkeys and mules require the dose of injectable drug to be ~ 30% higher than that used for the horse.

IV. Preoperative evaluation

- Emphasis should be placed on physical examination and recent history, and further testing should be based on the results of these findings.
- The personality of the donkey can make it difficult to determine if the animal is depressed or simply stoic.
- Differences exist in some laboratory values between donkeys and horses.
    - e.g. gamma glutamyl transferase is approximately 2–3 times higher in donkeys than horses.

V. Sedation

- The drugs used for sedation in horses can be used in donkeys and mules, but the dose usually has to be *significantly higher* to achieve the same effect.
- Some large unruly mules may have to be sedated with an intramuscular injection to allow safe handling and jugular catheter placement.
  - For this purpose, IM doses of *xylazine* (3 mg/kg), *detomidine* (0.04 mg/kg) or *romifidine* (0.2 mg/kg) plus or minus *morphine* (0.3 mg/kg) will provide effective sedation in about 20–30 min.
  - Once approachable, further IV sedation (e.g. α_2 agonist) may be given.
  - Common IV doses of sedatives include:
    - *Xylazine* (1.0–1.5 mg/kg).
    - *Detomidine* (0.02–0.03 mg/kg).
    - *Romifidine* (0.1–0.15 mg/kg).

VI. Induction of anesthesia

- As in the horse, a variety of drugs and drug combinations may be used.
- The drug regimens outlined below are only intended for *short-duration* procedures.

Ketamine (2.5–3 mg/kg, IV)
  - Administered following heavy sedation with an α_2 agonist.
  - Muscle relaxation is poor.
  - Duration of surgical anesthesia is short (5–10 min).
  - Premedication with *detomidine* or *romifidine* should give a longer duration of surgical anesthesia than *xylazine* premedication.

Ketamine (2.5–3 mg/kg, IV) + benzodiazepine (e.g. diazepam 0.05 mg/kg, IV)
  - Administered following heavy sedation with an α_2 agonist.
  - Improved muscle relaxation.
  - Probably doesn't increase the duration of surgical anesthesia.

Thiopental (5 mg/kg, IV)
  - Administered following heavy sedation with an α_2 agonist.
  - No analgesia with *thiopental*.

Tiletamine + zolazepam (1.25–2 mg/kg, IV)
  - Administered following heavy sedation with an α_2 agonist.
  - Use high end of dose range in smaller donkeys.
  - Longer surgical anesthesia than with *ketamine*.
  - Good inductions.
  - Recoveries not as good as with *ketamine*, but are acceptable.

VII. Maintenance of anesthesia

A. Inhalational anesthetics

○   May be used in the same manner as in the horse.
○   There is no reason to believe that MAC values differ significantly from those of horses.

B. TIVA

○   Alpha$_2$ agonist + *ketamine* in a solution of *guaiphenesin* are the most commonly used drugs.
–   *Guaiphenesin* is used primarily for muscle relaxation.
–   Care must be taken to avoid overdosing with *guaiphenesin*, especially when anesthetizing small donkeys.
■   It is probably never necessary to use more than a 5% solution even in the largest mules, and the solution should be further diluted before use in small donkeys.
○   The usual method is to induce anesthesia with the same α_2 agonist and *ketamine* and then administer the triple combination for maintenance.
–   A rough guide is to put the induction doses of the α_2 and *ketamine* in the *guaiphenesin* (0.5–1.0 liters) solution.
–   This should provide a surgical plane of anesthesia for about 30–40 min.

C. PIVA

○   As described for the horse.

VIII. Recovery from anesthesia

●   Recovery from anesthesia is usually smooth, particularly in donkeys.
●   The same care should be taken to protect the airway as in the horse.

IX. Analgesia

●   Evaluation of pain can be difficult (see Chapter 20).
●   Analgesics should be provided in the postoperative period.

A. NSAIDs

○   May be used for the treatment of acute or chronic pain.
○   May be combined with opioids for the treatment of acute pain.
○   Generally have a shorter elimination half-life than in the horse.
–   However, *carprofen* is metabolized more slowly in donkeys.
–   Miniature donkeys may metabolize some NSAIDs faster than do standard-sized donkeys.

B. Opioids

○ Safe to use at the horse dose for postoperative analgesia.
○ No information is available on their efficacy.
○ Ileus is a risk, even with short-term use.

Anesthesia of the geriatric horse

Lydia Donaldson

- A larger number of geriatric horses are presented nowadays for surgical or diagnostic procedures requiring general anesthesia than was the case two decades ago.
  ○ This may reflect their increasing status as companion animals.
- Due to concomitant or age-related disease and environmental factors there is a large variability in physiological status among the geriatric population.
  ○ Chronological age does not equal physiological age.
- The geriatric horse may not age in the same pattern as its human or small-animal counterpart because of its need to remain somewhat physically active in its day-to-day existence.
  ○ However, like the more sedentary species, perioperative risk for older horses is greater than that of 2 to 4-year-olds.

I. Definition of geriatric (see Table 15.1)

- Geriatric horses have traditionally been defined as those > 20 years of age.
- Students of gerontology use the following definitions:
  ○ *Life span*: the maximal attainable age for the species.
  ○ *Life expectancy*: the typical age attained by contemporary, average members of the species.
  ○ *Geriatric*: an individual that has survived to 75–80% life expectancy

Table 15.1   Definition of 'geriatric' equines in years.

	Horse	Pony
Life span	~ 35	~ 45
Life expectancy	~ 25	~ 35
Geriatric	19–20	26–28

II. Physiology of aging

- A gradual loss of functional reserve (i.e. the maximum capacity to perform in response to challenge or stress) occurs in most organ systems.
- The following information is primarily derived from studies in people. Evidence of similar changes in the geriatric horse is included where available.

A. Cardiovascular system

o Myocardial and arterial compliance are decreased and result in decreased ventricular filling and increased vascular resistance.
o Myocardial contractility is unchanged.
o Precision in baroreceptor responses is decreased.
o Responses to adrenergic stimulation are decreased:
   – Stress induces a smaller inotropic and chronotropic response.
   – The maximum heart rate of older horses is significantly less (190 versus 220) than that of young horses.
   – Larger doses of inotropes and vasoconstrictors are required to increase cardiac output or blood pressure.
o Cardiac dysrhythmias are more common.
   – In one report, 30% of horses > 20 years experienced a dysrhythmia during inhalational anesthesia compared with 16% of younger horses.

B. Neurological system

o Brain mass is decreased due to a loss of neurons.
o Neuronal networking and neurotransmitter concentrations are altered and lost.
o Autonomic and somatic reflexes and cognitive responses are slowed due to delayed central processing and decreased conduction velocity in afferent and efferent nerve fibers.

C. Respiratory system

o Elastin content of the lung is decreased, and fibrous connective tissue is increased resulting in decreased elastic recoil, increased residual volume, and increased closing capacity to above functional residual capacity.
o Alveolar surface area is decreased, and dead space ventilation and shunting are increased resulting in reduced efficiency of gas exchange.
o The mean PaO_2 of awake, geriatric horses is significantly less (90 versus 101 mmHg) than that of a comparable group of young horses.

D. Musculoskeletal system

o Skeletal muscle mass decreases, resulting in a lower basal metabolic rate which contributes to the observed decrease in maximal exercise capacity.
o Bone density decreases.

E. Body composition

o Adipose tissue is relatively increased.
o Lean body mass is relatively decreased.
o Total body water is decreased.
o The larger surface to mass ratio, decreased metabolic rate, and impaired thermoregulation predispose to *hypothermia*.

F. Hepatic and renal systems

- The decreased tissue mass ultimately results in decreased metabolic, excretory, and reabsorptive capacity.
- Glomerular filtration rate is decreased.
- Splanchnic and total renal blood flows are decreased.

III. Pharmacodynamics and pharmacokinetics

- Generally, geriatrics are more sensitive to anesthetics, and drugs have a longer duration of effect. (See Table 15.2.)
- Factors responsible for increased sensitivity to anesthetics include changes in:
  - Target receptor or neuronal density, receptor affinity, and neuronal subcellular response.
  - Cardiac output and cerebral blood flow.
  - Relative size and perfusion of central and peripheral compartments.
  - Drug metabolism and/or elimination.
  - Individual perceptions of pain.

Table 15. 2   Anesthetics and analgesics used in geriatric horses.

Anesthetic	Possible effect of aging	Concerns
Alpha$_2$ agonists	• Fewer adrenergic receptors peripherally and centrally • Delayed hepatic metabolism	• Arrhythmias, prolonged action and side effects (bradycardia, hypotension, ataxia)
Phenothiazines	• Delayed hepatic metabolism and renal excretion	• Unresponsive hypotension
Opioids	• Increased sensitivity • Morphine clearance decreased	• Increased incidence of adverse effects (dysphoria, pacing, hypertension)
Benzodiazepines	• Increased sensitivity and decreased clearance	• Prolonged action delaying full behavioral recovery
NMDA antagonists	• Fewer NMDA receptors. Decreased hepatic metabolism and clearance	• Prolonged action causing rough emergence
Inhalant anesthetics	• Increased sensitivity	• Accentuated hypotension
Guaiphenesin	• Decreased hepatic metabolism and clearance	• Prolonged action causing weakness in recovery
Atracurium	• Not affected	
Local anesthetics	• Increased sensitivity • Greater cranial epidural spread • Lower toxic dose	• Unexpected recumbency after epidural or signs of toxicity (muscle fasciculations, tachycardia, seizures)

IV. Common indications for anesthesia of the geriatric horse

A. Gastrointestinal emergencies

○ Small intestinal strangulation/obstruction (often caused by lipomas) and impaction may be more common in older horses.
○ Primary concerns are similar to those of any horse with an acute abdomen.

B. Neoplasia

○ Horses with operable neoplasia (e.g. squamous cell carcinoma, superficial melanoma) are usually otherwise healthy.

C. Sinusitis and ethmoid hematomas

○ These tend to occur, more commonly, in older horses but are localized disease processes in healthy horses.
    – Concerns might include anemia of chronic disease or blood loss.

D. Ocular procedures

○ Corneal debridement or repair, conjunctival flap, cataract removal and enucleations are not usually undertaken in severely debilitated horses.
○ Neuromuscular blockade may be needed to immobilize the globe for intraocular surgery.
    – The dose and duration of action of *atracurium*, the most commonly used agent in the horse, is not affected by age in humans.

E. Esophageal choke

○ The poor dentition that is responsible for the choke is a chronic condition and these horses are often emaciated and dehydrated.
○ Pharyngeal reflexes are slowed in geriatrics and aspiration pneumonia may be more likely to occur in the choked geriatric than in younger horses.
○ Pre-anesthetic evaluation and stabilization are important.

F. Trauma

○ Lacerations involving the hoof, synovial structure, tendons or fractures generally occur in otherwise healthy individuals.
○ Pre- and postoperative pain management should be an important component of patient care.

V. Clinical approach to anesthetizing the geriatric equine

A. Preanesthetic evaluation

- ○ Obtain a history of general activity, exercise tolerance, and ability to rise from recumbency.
- ○ Physical examination including assessment of general body condition.
- ○ Complete blood cell count and chemistry.
  - – Studies have failed to identify clinically significant differences in hematological and serum biochemical values between healthy geriatric and young horses.
- ○ Complete cardiac evaluation is required if murmurs or arrhythmias exist.

B. Sedation and premedication (see Table 15.2)

Acepromazine (~ 0.02 mg/kg, IM)
- ○ Large doses in horses with decreased cardiovascular reserve may result in significant hypotension.
- ○ Small doses may protect against arrhythmias and improve cardiac output by decreasing afterload.
  - – Low doses may be combined with an α_2 agonist.

Xylazine (0.4–1.0 mg/kg, IV)
- ○ It is advisable to start with a low dose, and then dose to effect to avoid excessive bradycardia and ataxia.
- ○ Longer acting, more receptor specific α_2 agonists (e.g. *detomidine*, *romifidine*, *medetomidine*) may have excessively long durations of action and more adverse effects.

Butorphanol (~ 0.01 mg/kg, IV)
- ○ Elderly people require smaller doses of opioids and this may be the case in horses.
  - – Conservative dosing should be used when adding an opioid to α_2 agonists.

C. Induction

- ○ Titration to effect (to accommodate age-related decreases in dose requirements) may be desirable, but the size of the horse and potential for injury make this method impractical in standard-sized horses.
  - – *Guaiphenesin* may be the exception.
- ○ Bolus intravenous injection of a calculated dose of induction drugs is required to achieve a rapid transition from consciousness to stage III anesthesia.
- ○ Examples include the following:

Ketamine (~ 2 mg/kg, IV)
- ○ Delayed recovery has been observed in elderly humans and horses.

Diazepam/midazolam (~ 0.05 mg/kg, IV) + ketamine (~ 2 mg/kg, IV)
- ○ A single bolus for a short procedure may result in a longer than expected period of recumbency as benzodiazepine dose requirements and clearance are decreased in geriatric humans.

Guaiphenesin (~ 50 mg/kg, IV) + ketamine (~ 2 mg/kg, IV)
- o   The advantage of *guaiphenesin* is that it can be given to effect, thus reducing the chance of overdose and prolonged action.
- o   Clearance may be decreased, and residual *guaiphenesin* or its active metabolite may contribute to weakness in recovery after short procedures.

D. Maintenance

Ventilation
- o   Should be assisted.
  - –   Respiratory muscle function and chest wall compliance decrease with aging.
  - –   Geriatric lungs have less efficient gas exchange.
  - –   Recumbency exacerbates this problem and also increases the potential for hypoventilation.

Inhalational anesthesia
- o   MAC is likely to be lower in geriatric horses.
  - –   In a clinical study, the end-tidal concentration of halothane and isoflurane was significantly less in a group of 100 geriatric horses compared with that of a matched group of younger horses.
- o   *Halothane* is the *least appropriate* inhalational agent due to its cardiovascular depressive actions, arrhythmogenicity, hepatic metabolism, potential hepatotoxicity, and greater blood solubility.

Total intravenous anesthesia (see TIVA)
- o   Increased sensitivity and greater drug accumulation (delayed metabolism and clearance) should permit the use of lower doses at longer intervals or a lower rate of infusion.
- o   Recovery may be prolonged, but its quality should be good.

Balanced anesthesia (see PIVA)
- o   Combining low doses of inhalational agent and IV anesthetics to reduce the adverse effects of both may be particularly applicable to the geriatric equine.
- o   Care should be taken if a constant rate infusion of *lidocaine* is added as sensitivity and toxicity may be increased.

Local anesthetics
- o   Perineural infiltration at the surgical site allows administration of lower doses of the more compromising general anesthetics.

E. Monitoring

Positioning
- o   Careful positioning to protect against nerve or muscle injury is particularly important for old horses with reduced muscle mass and neuromuscular function.

Blood pressure
- o   With reduced total body water and cardiovascular functional reserve, geriatrics may be susceptible to hypovolemia and require greater cardiovascular support.

Electrocardiography
- o The increased incidence of dysrhythmias in anesthetized older horses dictates careful monitoring.

Blood gas analysis
- o Geriatrics may be at greater risk of hypoxemia.

Body temperature
- o Decreased metabolic rate and muscle mass predispose to hypothermia.

F. Recovery

- o Old horses frequently require assistance in getting to their feet due to:
  – Reduced muscle strength.
  – Widespread degenerative joint disease.
  – Decreased neuromuscular control.
- o Sedation (0.01–0.02 mg/kg *xylazine*, IV) may be necessary as older horses are often opinionated and may be determined to stand before they are ready.

VI. Age-associated diseases and anesthesia

A. Recurrent airway obstruction

- o Small airway obstruction and loss of alveolar surface area interfere with ventilation, ventilation/perfusion distribution, and diffusion.
- o Assisted ventilation with insufficient expiratory time may result in air trapping and hyperinflation of the lung.
  – Permissive hypercapnea may be necessary to optimize gas exchange.
- o Long-term administration of β_2 adrenergic bronchodilators may contribute to muscle weakness in recovery.
  – There is evidence that long-term use of β_2 agonists may affect muscle spindle control in humans, and anecdotal evidence that this may also occur in horses.

B. Equine Cushing's disease

- o Muscle loss, increased body fat, lethargy, tachycardia, hypertension, fluid and electrolyte imbalances, immuno-suppression predisposing to pneumonia, corticosteroid-induced hepatopathy, and osteoporosis will potentially contribute to increased anesthetic challenges.
- o Cardiovascular instability and possibly greater sensitivity to anesthetics may occur.
- o Dopamine agonists and serotonin antagonists used to treat Cushing's disease may cause hypotension and arrhythmias, and alter mentation.

C. Hypothyroidism

- o The clinical diagnosis of hypothyroidism is based on observing muscle weakness and loss, increased body fat, lethargy, and decreased thyroid hormones.

○ Resting heart rate, cardiac output, respiratory rate, and body temperature may be decreased in extreme cases.

○ Bradycardia, inadequate tissue perfusion, and further decreases in anesthetic requirement may occur.

D. Aortic valve insufficiency

○ Is more common in older horses.

○ It is the most common of the degenerative valvular cardiac diseases.

○ Congestive heart failure is not a common clinical condition in horses.
  – It is usually life threatening and therefore not likely in horses presented for general anesthesia.

○ Cardiac performance should be fully evaluated before anesthesia.
  – Significant left heart enlargement or decreased fractional shortening indicate borderline function and owners should be advised of the additional risk.

○ Minimize the negative impact of anesthetics on contractility by careful selection of drugs and doses.

○ Optimize forward flow by decreasing arterial vascular tone.

○ Optimize venous return by the judicious use of fluids.

Anesthesia and pregnancy

Lydia Donaldson

● The need for anesthesia during pregnancy occurs under two general conditions:
  ○ Surgical procedures unrelated to the pregnancy.
  ○ Obstetrical procedures.

● Although the overall concerns are similar, obstetrical procedures must also focus on the delivery of a *viable foal*.

● Maintaining maternal blood pressure and oxygenation are critical under both circumstances, but minimizing fetal exposure to longer acting, compromising anesthetic agents is also important for success.

I. Physiology of pregnancy (see Table 15.3)

● The following observations are from studies of pregnant women. Information regarding pregnant mares will be included where available.

A. Cardiovascular

○ PCV, hemoglobin, and total protein (albumin more than globulin) are decreased due to dilution.
  – This is secondary to the relatively greater increase in plasma volume than red cell mass or protein.

○ Blood pressure may be normal or slightly below normal.

Table 15.3 Physiological changes identified during pregnancy in women.

Cardiovascular	↑ Plasma volume (~40%)
	↑ Red blood cell mass (~20%)
	↑ Ventricular end-diastolic volume and wall thickness
	↑ Fractional shortening and stroke volume (20–50%)
	↑ Resting heart rate (20–30%)
	↑ Cardiac output (30–50%)
	↓ Systemic and pulmonary vascular resistance (20–30%)
	↑ Procoagulant activity
Respiratory	↑ Metabolic rate
	↑ Minute ventilation (70%)
	↓ Functional residual capacity (20%)
	↑ Closing volume
	↓ $PaCO_2$ (30%), increased pH and normal PaO_2
Renal	↑ Blood flow
	↑ Glomerular filtration rate
Uterus	↑ Blood flow
	Altered vascular responses to catecholamines
Brain	↑ Progesterone and endogenous opioids

- Procoagulant activity is increased.
  - In pregnant mares, increases occur in fibrinogen, Factor VIII: C, and von Willebrand factor.

B. Respiratory

- There is a greater potential for hypoxemia due to increased O_2 consumption, decreased functional residual capacity, and increased closing volume.
- Total O_2 transport is greater due to:
  - Respiratory alkalosis increasing O_2 uptake at the lung.
  - Greater total hemoglobin.
  - Increased cardiac output.
- Fetal O_2 uptake is facilitated by:
  - Increased O_2 delivery.
  - Higher maternal 2,3-DPG facilitating O_2 unloading at the placenta.
  - A lower P_{50} for fetal hemoglobin (although not structurally different from adult hemoglobin).

C. Renal

- Increased renal blood flow, glomerular filtration rate, and plasma result in decreased serum blood urea nitrogen and creatinine.

D. Uterus

- Uterine blood flow is increased.

    ○ Uterine vascular control is altered.
- – Alpha$_1$ adrenoceptor mediated vasoconstriction is increased.
- – Alpha$_2$ adrenoceptor mediated vasodilation (nitric oxide mediated) is enhanced.
- – Beta$_2$ adrenoceptor mediated vasodilation is reduced.

II. Factors affecting drug disposition during pregnancy

A. Maternal

○ Increased plasma volume dilutes the anesthetic agent.
○ Decreased serum albumin increases the *free* fraction of protein-bound drugs.
○ Increased body fat provides a larger redistribution compartment.
○ Increased pulmonary blood flow, minute ventilation, and decreased functional residual capacity hasten the uptake and elimination of less soluble inhalants.
○ Increased circulating progesterone and endogenous opioids are partly responsible for the observed MAC decrease for inhalants, and dose decreases for local anesthetics, as well as some sedatives and analgesics.
○ Greater cranial spread of epidurally administered local anesthetics or analgesics.
- – The epidural space is reduced in volume due to blood volume increases causing vertebral venous engorgement.
- – This increases sensitivity to local anesthetics.

B. Placental

○ The equine placenta is relatively primitive.
- – The capillary-to-capillary distance is very small (~12 μm) within the micro-cotyledons.
- – Capillary bed flow of the two circulations is countercurrent.
○ In the pregnant mare, uterine blood flow is approximately twice that of umbilical blood flow.
- – *Uterine blood flow* is affected by factors that influence cardiac output and blood pressure (e.g. inotropes, vasopressors, vascular volume, anesthetic drugs, autonomic nervous system activity, etc).
- – *Uterine vascular resistance* is affected by a number of factors (e.g. hypoxemia, hypercarbia and extreme hypocapnia, stress, pain, anesthetic drugs).
○ Maternal to fetal drug exchange across the lipoprotein barrier occurs by *diffusion*.
- – It is dependent on the concentration gradient, lipid solubility, ionization and size of the molecule.
○ The placenta has metabolic activity (e.g. cytochrome P$_{450}$, several transferases, sulfating enzymes).

C. Fetal

○ The equine fetal circulation does not include a *ductus venosus*.
- – Thus, all umbilical venous blood flows through the liver sinusoids before reaching the right ventricle.
○ Fetal albumin concentration is ≥ than that of the mare (2.3−4.2 mg/dl).

○ Anesthetics reaching the fetal brain are diluted by the 50–60% of cardiac output that does not flow through the placenta, some hepatic metabolism, and mixing with left ventricular blood through the ductus arteriosus.

○ The fetal blood–brain barrier is immature allowing more direct access.

○ Fetal heart rate is *increased* by factors such as adrenosympathetic response, acidosis, slow-onset hypoxia, activity, atropine and *acepromazine*.

○ Fetal heart rate is *decreased* by factors such as acute hypoxia, acidosis, sleep, α_2 agonists, and opioids.

III. Anesthesia concerns in the pregnant mare

A. Compression of the vena cava

○ It is sometimes recommended that mares undergoing Cesarian section *not* be placed squarely on their backs as this may result in life-threatening hypotension from compression of the caudal vena cava.

– However, there is no convincing evidence that tilting is beneficial in horses, and tilting the mare to one side is going to increase the likelihood of myopathy.

B. Hypoventilation, hypoxemia, and impaired gas exchange

○ Hypoventilation resulting from the effects of anesthesia and recumbency is compounded by the gravid uterus impinging on the diaphragm, further reducing thoracic volume and compliance.

○ Reduced cardiac output, atelectasis, and decreased thoracic compliance contribute to ventilation/perfusion mismatch and shunt.

C. Myopathy

○ The risk is greater due to the increased body mass and increased likelihood of hypotension and hypoxemia.

D. Recovery

○ Brood mares are often older, overweight or heavy with their pregnancy, arthritic, unfit, and less dependent on man than the average horse in training.

○ These factors contribute to difficulty getting to their feet and being uncooperative during recovery.

IV. Anesthetic management in pregnancy

• Drugs given to the mare can affect the fetus either *directly*, by crossing the placenta to alter neurological or cardiovascular function, or *indirectly* by altering uterine blood flow.

• In general, molecules that cross the blood–brain barrier also cross the placenta.

• Equine fetal stress is indicated by persistent bradycardia and an increase followed by a decrease in activity.

A. Sedation and premedication

Acepromazine
- o Fetal and maternal heart rates increase for ~ 25 min after *acepromazine* (0.1 mg/kg, IV) administration to the mare.
- o Fetal aortic blood flow does not change at this dose.

Alpha$_2$ agonists
- o Have proven to be clinically safe, although fetal bradycardia is as profound as and of longer duration than maternal bradycardia.
- o Fetal aortic blood flow decreases 66% after *detomidine* (10 µg/kg, IV) is administered to the mare.
- o *Detomidine* decreases spontaneous uterine contractility in late pregnancy.

Opioids
- o Readily cross the placental barrier.
  - – Increased fetal activity was reported in pony fetuses after *pentazocine* administration to the mares.

Flunixin meglumine
- o Blocks PGF$_{2\alpha}$ release and protects against fetal loss after uterine manipulation.
- o Near term, NSAIDs can mediate premature ductus arteriosus closure resulting in pulmonary hypertension.

B. Induction

Ketamine
- o Has *no* cardiovascular effects on the fetus.
- o Decreased responsiveness and muscle rigidity have been seen in human neonates at birth.

Diazepam
- o Has been reported to cause depression, hypothermia and hypotonia in human neonates after maternal pre-partum dosing.

Midazolam
- o Does not accumulate in the fetus but may cause respiratory depression in the neonate.

Guaiphenesin
- o Readily crosses the placenta.
  - – Nevertheless, it has been successfully used in TIVA for controlled vaginal delivery, as well as induction and maintenance for Cesarean delivery of viable foals.

C. Maintenance

- o Positive pressure ventilation and supplemental O$_2$ should be used to prevent hypoventilation and hypercapnia and to optimize oxygenation, regardless of the anesthetic technique.

Inhalational anesthetic MAC
- o Pregnancy reduces MAC 25–40% in other species, so a significant reduction would be expected in the late-term mare.
- o Inhalational agents dose-dependently decrease maternal blood pressure, cardiac output, uterine blood flow, uterine tone and contractile activity.
- o Umbilical blood flow and fetal blood pressure are also decreased, but pH is maintained in procedures lasting less than an hour.

TIVA
- o *Guaiphenesin/ketamine/detomidine* maintains maternal blood pressure and uterine blood flow better than *halothane*, but fetal bradycardia is comparable.

Balanced anesthesia
- o Has not been studied in pregnant mares.
- o A constant rate infusion of *lidocaine* may be added with caution, as increased sensitivity and a lower toxic threshold for local anesthetics has been noted with pregnancy.

D. Specific monitoring

Direct blood pressure
- o Measurement of blood pressure is critical to ensure sufficient driving pressure for uterine perfusion.

Arterial blood gas analysis
- o Helps to optimize uteroplacental O_2 delivery.
- o Hypoxemia and hypercapnia activate the sympathetic nervous system causing uterine artery constriction.
- o Hypocapnia decreases cardiac output and increases uterine vascular resistance.

Electrocardiography
- o Allows detection of dysrhythmias which could compromise cardiac output and uterine blood flow.

Fetal heart rate (FHR)
- o Is an indicator of fetal well-being and can be detected as early as the 120th day of pregnancy.
- o Positioning or surgical manipulations prohibit ECG lead placement for FHR monitoring, but pre- and postanesthetic readings may be informative of fetal status.
- o Heart rate is decreased by:
  - Acute onset hypoxemia.
  - Acidosis.
  - Sleep or the direct effect of sedatives, anesthetics or analgesics.
- o Heart rate is increased by:
  - Slow onset hypoxemia or recovery after acute hypoxemia.
    - ■ This activates the fetal adreno-sympathetic system causing increased FHR and blood pressure.

E. Cardiovascular supportive measures

- ○ *Ephedrine* improves cardiac output and causes no decrease in uterine blood flow.
  - – *Dobutamine* and *dopamine* are also satisfactory.
- ○ *Atropine* crosses the placenta whereas *glycopyrrolate* does not.
- ○ For uterine surgery, intensive fluid therapy may be necessary to compensate for blood loss, particularly with inhalational anesthesia where decreased uterine tone hinders hemostasis.

F. Recovery

- ○ Oxygen should be administered by demand valve and/or insufflation.
- ○ The heavily pregnant, unfit, older mares may need assistance.
- ○ Those that have been in labor for a long time will also be exhausted.
- ○ Following Cesarean or controlled vaginal delivery, care should be taken to dry the recovery stall floor of amniotic fluids and obstetrical lubricant.
- ○ Multiparous mares delivered of their foal often emerge from general anesthesia anxiously searching for it.

G. Pain management

- ○ The long-term administration of analgesics during the first trimester of pregnancy may alter normal fetal development, and during later pregnancy may induce tolerance in the fetus with withdrawal after delivery.
- ○ Epidural opioids have minimal maternal or fetal cardiovascular effects during late pregnancy.

V. Managing anesthesia in the pregnant mare

- ● *Elective surgery* should be avoided. If this is not possible, the mare and fetus are at the least risk during the middle trimester, i.e. after differentiation and development of the fetus but before rapid growth burdens the mare.

A. Non-obstetrical procedures

Abdominal surgery for intestinal emergency
- ○ Short-term survival rate of pregnant mares with surgical colic (61%) is reported to be no different from that of non-pregnant horses (65%).
- ○ Fetal loss (12%) is comparable regardless of the stage of pregnancy.
  - – It is linked to maternal endotoxemia and to hypoxemia and/or hypotension in mares <60 days to term.
- ○ Uterine manipulation in early equine pregnancy frequently results in fetal loss.
- ○ Attentive volume support, preoxygenation, mechanical ventilation and maintenance of blood pressure and oxygenation are important as with any colic case.
  - – Hypovolemia may be less easily identified in the pregnant mare due to expanded blood volume and dilutional anemia and hypoproteinemia.

Trauma
- o Many wounds, fractures, ocular injuries, etc. require induction of anesthesia regardless of the stage of pregnancy.
- o The stress of these injuries, as with abdominal surgery, may be as detrimental to pregnancy as are anesthesia and surgery.

B. Obstetrical procedures

Uterine torsion
- o A 70% survival rate has been reported for the mare and fetus.
- o Rotation of the uterus on its long axis compromises perfusion.
- o Correction of the torsion may be done with the mare standing, through a flank incision, or may require general anesthesia with rolling or celiotomy.
- o Anesthetic concerns are those of non-obstetrical late-term procedures plus any hemodynamic instability caused by uterine manipulation during surgery or additional cardiopulmonary compromise created by lifting and rolling the heavily pregnant mare.

Dystocia/Cesarean section (see Table 15.4)
- o Mare survival-to-discharge rates for dystocia, whether resolved by vaginal or Cesarean delivery, are 80–90%.
- o Foal survival varies from 11 to 30%, with time from onset of labor to delivery being a significant factor in foal outcome.
- o Elective Cesarean section has considerably better survival rates: 100% of mares and 90% of foals.

Table 15.4 Suggested general anesthetic management of a mare with a live foal dystocia for controlled vaginal delivery or Cesarean section.

- All members of the team must be prepared and understand the need for efficiency
- Pre-medicate with low dose *xylazine* (0.4 mg/kg, IV) ± *butorphanol* (0.01 mg/kg, IV)
- Insufflate O_2 as soon as the mare will tolerate it
- Induce with *guaiphenesin* infusion to effect (40–50 mg/kg, IV) and *ketamine* (2 mg/kg, IV)
- Assist ventilation with 100% O_2 by demand valve when mare is intubated
- *Sevoflurane* or *isoflurane* at MAC (or below if possible) until the foal is delivered then increase as necessary
- During Cesarean section and if the mare is stable, the vaporizer may be turned off several minutes before the foal is delivered
- Initiate positive pressure ventilation but do not hyperventilate as $PaCO_2 < 30$ mmHg adversely affects cardiac output and uterine blood flow
- Analyze arterial blood gas as soon as an arterial catheter is placed for direct blood pressure monitoring
- If a Cesarean is needed, consider more intensive volume support in anticipation of uterine blood loss
- Oxytocin will help control uterine bleeding but may cause vasodilation if given too rapidly
- Do not administer unless there is adequate (> 30 min) time for slow infusion
- In recovery, assist ventilation and supplement O_2 with a demand valve and continue IV fluids, if necessary, and as permitted by the emerging mare
- Discourage premature efforts to stand with sedation and manual restraint
- Be prepared to assist recovery with head and tail support (ropes, manual)
- Dry recovery floor of amniotic fluids, blood and obstetrical lubricant

Live foal at presentation
- o Efforts at delivery should proceed rapidly from a quick assessment of the standing mare to assisted delivery to general anesthesia with controlled vaginal delivery or Cesarean section.
- o Efforts should be made to minimize fetal exposure to anesthetics by choosing agents that do not accumulate in the fetus, limiting the time between induction and delivery, and dosing to effect.

Dead foal at presentation
- o Stabilizing the mare becomes as important as removing the fetus.
- o Once the mare is rehydrated, with electrolytes and acid–base status corrected, the above steps should proceed in an orderly fashion.
- o Controlled vaginal delivery often involves *raising the mare's hindquarters* to shift the fetus back into the abdomen for repositioning. This places an additional load on the diaphragm and lungs and encourages abdominal venous return if the gravid uterus is not occluding the caudal vena cava.

Oxytocin administration intraoperatively
- o *Oxytocin* should be administered *slowly* to avoid vasodilation and hypotension.

Remote capture of equids

Nigel Caulkett

- ● Remote drug delivery can facilitate sedation or anesthesia of equids.
- ● Remote delivery is generally a last resort in domesticated horses, but is a commonly used technique to facilitate capture of wild equids.

I. General considerations

A. The decision to use remote delivery

- o Remote delivery can be used at distances of 1–40 meters.
- o Remote delivery will facilitate drug delivery in situations in which:
  - – An animal cannot be closely approached for safety reasons.
  - – The flight distance is such that the drug cannot be delivered via hand injection.
- o The decision to use remote delivery must be weighed against the risk, and the least traumatic technique should be used.

B. Trauma reduction

- o Trauma from remote delivery equipment is related to:
  - – The energy of the dart impact.
  - – The speed of drug injection.
  - – The injection site.

o Impact energy is described by the following equation:

$$KE = \frac{M}{2} \times V^2$$

where KE = Kinetic energy

M = Mass of the dart

V = Velocity

o From the above equation it is apparent that *velocity* is the major factor influencing trauma to the animal.

– A good general rule is to use the lowest velocity that will result in an accurate trajectory at a given distance.

o Drugs should be delivered into a *large muscle mass* to facilitate uptake and decrease the risk of trauma.

– The muscles of the thigh, neck, or shoulder are generally considered to be good locations for dart placement.

o Using large injectate volumes in association with high velocity is more likely to induce trauma.

– Ideally, low volumes (< 5 ml) should be delivered via slow, pneumatically powered injection, to reduce the risk of trauma.

C. Planning

o Anesthesia can be hazardous in field situations; therefore, appropriate supportive care, trained personnel, and emergency drugs and equipment should be readily available.

o With client-owned animals the client must be informed of the increased risk of morbidity and mortality when remote capture is used.

II. Equipment

A. Choice of delivery equipment

Distance

o *Pole syringes* can be used to extend the reach by up to 4 meters.

o *Blowpipes* can be used for distances up to 10 meters.

o *Pistols* are generally effective up to 20 meters.

o A *rifle* (pneumatic or cartridge powered) is required for >20 meters.

Trauma

o The least traumatic technique should always be chosen.

o Blowpipes and pole syringes deliver drugs at a low velocity; they are often preferable in close-range situations.

Familiarity with equipment

o Practice with equipment is vital to ensure accurate dart placement and to reduce the risk of trauma.

B. Equipment options

Pole syringe
- o Most useful for ranges of 1–3 meters.
- o Is typically used to deliver drugs to confined animals or to 'top up' anesthesia in recumbent but *lightly* anesthetized animals.
- o Generally, short, 14–16 gauge needles should be used, as this will decrease the risk of a needle hitting bone.
    - – This also decreases the risk of bending or breaking the needle.

Blow pipe
- o Is useful as a short-range (5–10 meters), limited-volume (3–5 ml) system.
- o Blowpipe darts cause minimal impact damage.
- o The discharge mechanism in most blowpipe darts is compressed air or butane.
    - – This results in low-velocity injection and minimal tissue trauma.
- o Practice is vital to ensure accurate dart delivery.

Pistols
- o Generally useful up to 20 meters.
- o Compact and easy to transport.
- o Projection of the dart is powered by compressed air or CO_2.
- o The maximum dart volume is generally 5 ml.

Rifles
- o Useful within ranges of 20–40 meters.
- o Compressed air, CO_2, or a .22 caliber cartridge powers projection of the dart.
- o Dart volumes of up to 10 ml may be delivered.
- o Velocity adjustment is via *pressure selection* in pneumatic rifles, and via *charge selection* or a *velocity dial* in cartridge-powered rifles.

III. Pharmacology

A. Choice of drug(s)

- o Drug(s) must be potent enough to be delivered in small volumes.
- o Must be stable in solution with other capture drugs.
- o Ideally, a drug(s) should confer a rapid, smooth induction and have minimal cardio-vascular and respiratory effects.
- o The ability to be reversed is desirable.

B. Alpha$_2$ agonists and antagonists

- o Alpha$_2$ agonists may be used to induce sedation of fractious horses or to facilitate capture of feral domestic horses or wild horses.

Xylazine
- o Useful for sedation or to improve muscle relaxation when combined with potent narcotics or dissociative agents.
- o The major limitation to its use is its low concentration (i.e. high volume requirements).

Detomidine
- o Better suited to remote delivery, as it is more potent.
- o Volume requirements are decreased compared with *xylazine*.

Romifidine
- o Has been used in combination with *Telazol*® for immobilization.

Medetomidine
- o The most useful α_2 agonist for remote delivery due to its potency.
- o Concentrations of 10–20 mg/ml are ideal for remote delivery.

Yohimbine (0.1–0.2 mg/kg) or tolazoline (2 mg/kg)
- o May be used to antagonize *xylazine*, *romifidine* and *detomidine*.

Atipamezole
- o To antagonize *medetomidine*, 2–4 times the *medetomidine* dose is required.

C. Phenothiazines

- o *Acepromazine* (0.05 mg/kg) can be used as an adjunct to α_2 agonists.

D. Opioids and opiates

Morphine
- o Can be used in combination with *detomidine* ± *acepromazine* to facilitate sedation of fractious horses.
- o Dose: 0.1–0.2 mg/kg, IM.

Butorphanol
- o May be substituted for *morphine*.
- o Dose: 0.025–0.05 mg/kg, IM.

Carfentanil
- o Can be delivered at a small volume and is readily reversible with *naltrexone*.
- o It is useful for capture of *wild* horses.
- o *Carfentanil* is typically combined with *xylazine* to improve muscle relaxation.

Etorphine
- o Has proven useful for immobilization of wild and domestic horses.
- o It should be combined with *acepromazine*, *azaperone*, or an α_2 agonist to decrease muscle rigidity.

E. Dissociative anesthetics

Ketamine
- o Is useful in combination with *medetomidine*.
- o Large volumes are required when it is combined with *xylazine*.

Telazol® (Zoletil®)
- o Is a combination of *tiletamine* and *zolazepam*.
- o The powered form can be reconstituted with an α_2 agonist to produce a satisfactory combination for capture of feral horses.

IV. Monitoring and supportive care

A. Field anesthesia

- o Increases risk.
  - – Down-time should be minimized.
  - – Supportive care should be provided.

B. Monitoring

- o Monitoring of pulse and respiration should be performed every 5 minutes.
- o Pulse oximetry assesses hemoglobin saturation and guides O_2 therapy.
- o Non-invasive blood pressure monitoring can be useful to monitor trends.

C. Oxygenation

- o The simplest way to provide supplemental inspired O_2 is nasal insufflation.
- o An ambulance-type regulator is sturdy and simple to use in the field.
  - – E or D cylinders can be transported to most field situations.
- o Flows of 8–15 liters/min are generally required for mature horses.
  - – Flow can be adjusted to the minimum that maintains a Hb saturation of 95–97%.

D. Position and padding

- o Generally, dorsal recumbency should be avoided as V/Q mismatching is most pronounced in this position and will contribute to hypoxemia.
- o If intubation is not performed, ensure head and neck extension to maintain a patent airway.
- o The horse should be maintained on a soft, level surface.
- o The legs may be hobbled or tied to prevent injuries to handlers during light anesthesia.
  - – Control of the limbs is particularly important with narcotic-based anesthesia.

V. Sedation of fractious horses

A. The decision to use IM sedation

- o Generally IM sedation is considered when IV drug administration will put handlers at significant risk of injury.
- o Drugs may be delivered via a *pole syringe* or *blow dart* to penned animals.
    - – Longer-range delivery equipment may be required in the field.
- o IM sedation can be used to facilitate IV delivery of additional sedatives or to facilitate delivery of IV anesthetics.

B. Sedative protocol

- o A mixture of *detomidine* (20–40 μg/kg) + *morphine* (0.1–0.2 mg/kg) is administered by IM injection.
    - – Ideally, *morphine* should be used at a concentration of 50 mg/ml to facilitate low-volume delivery.
- o *Acepromazine* (0.05 mg/kg) can be combined with this mixture.
    - – For breeding stallions the risk of priapism should be discussed with the owner.
- o The horse should be left alone to facilitate drug uptake and sedation.
- o After 15–20 min, approach the horse cautiously and handle if possible.
    - – Additional *detomidine* (5 μg/kg, IV) will provide further sedation if necessary.
- o If anesthesia is the goal, the horse can be induced with *diazepam* (0.1 mg/kg) + *ketamine* (2 mg/kg).
- o The horse should be watched for at least 2 hours after drug administration, as there is a risk of CNS stimulation if the *detomidine* is metabolized prior to the *morphine*.
    - – Additional *detomidine* or *acepromazine* can be used to treat excitement.
    - – Alternatively, *butorphanol* (0.05 mg/kg) may be substituted for *morphine*, but sedation will be less profound.

VI. Remote capture of feral horses

A. Techniques

- o Physical capture may be possible with well trained wranglers.
- o Depolarizing muscle relaxants (*succinylcholine*) have been used to facilitate capture, followed *immediately* by anesthesia.
    - – *There are risks of respiratory depression and humane issues involved with this technique.*
- o *Telazol*®-based protocols are probably the most readily available and user friendly.

B. Telazol® and alpha$_2$ mixtures

- o *Telazol*® can be reconstituted with an α_2 agonist to decrease volume.

- ○ *Telazol®* (3.5 mg/kg) + *butorphanol* (0.07 mg/kg) + *xylazine* (3 mg/kg) has been used successfully to capture feral horses.
  - – The volume is large, but it is possible to reduce it considerably if concentrated *xylazine* (300 mg/ml) is available.
  - – This combination is more readily available to the general practitioner than potent narcotics.
- ○ Alternatively, *Telazol®* (2 mg/kg) + *detomidine* (80 µg/kg) has been advocated.

C. Carfentanil and xylazine

- ○ *Carfentanil + xylazine* has been used successfully to immobilize a variety of wild equids.
- ○ Results in the domestic horse have *not* been favorable.
  - – *Carfentanil* (0.015 mg/kg) + *xylazine* (1 mg/kg) was studied in domestic horses.
  - – The combination produced tachycardia, hypertension, hyperthermia, and death from pulmonary edema in one horse.

VII. Wild equids

A. Techniques

- ○ In general, remote delivery is required for capture of wild equids.
- ○ Drug choice will depend on availability of drugs and supportive care.
- ○ It is important to note that drug doses are generally greater in free-ranging animals compared with captive animals.

B. Zebra

- ○ A variety of combinations have been advocated, many of which are narcotic based.
- ○ Supplemental O_2 should be provided as hypoxemia is common with all combinations.

Adult Grevy's zebra
- ○ *Etorphine* (6 mg) + *acepromazine* (25 mg) induces anesthesia and can be antagonized with 2 mg *diprenorphine*/mg of *etorphine*.
- ○ *Carfentanil* (12 mg total) + *detomidine* (13 mg total) may also be used.
  - – Immobilization with this combination should be antagonized with 100 mg of *naltrexone*/mg of *carfentanil*.

Common zebra
- ○ *Etorphine* has also been recommended.
- ○ *Etorphine* can be combined with *azaperone* (80 mg total).
  - – *Males*: Total of 6 mg *etorphine*.
  - – *Females*: Total of 4 mg *etorphine*.

Non-narcotic protocol
- ○ If desired, a captive zebra can be immobilized with:
  - – *Telazol®* (1.8 mg/kg) + *romifidine* (0.35 mg/kg).

C. **Przewalski's horse**

- o *Medetomidine* (0.1 mg/kg) + *ketamine* (2 mg/kg)
- o Provides effective anesthesia.
  - – *Atipamezole* is recommended for antagonism of immobilization.
  - – Dose: 0.3 mg/kg split IV (25%) and subcutaneously (75%).
  - – Transient hypoxemia and bradycardia were noted with the above protocol.

Carfentanil
- o Has been used alone (0.02 mg/kg).
- o Supplemental *ketamine* or *guaiphenesin* is required in some cases to induce suitable anesthesia.

Telazol® (3.3 mg/kg) + romifidine (0.6 mg/kg)
- o This combination may also be used.

16   Anesthesia of the limbs

Jim Schumacher and Fernando A. Castro

I. Indications

- Regional anesthesia is used primarily to:
  - Localize the site of pain causing lameness.
  - Provide anesthesia for surgery performed with the horse conscious and standing.
  - Provide adjunctive analgesia for anesthetized horses undergoing surgery.
  - Provide temporary analgesia (e.g. for horses with laminitis).

II. General principles

A. Local anesthetic drug selection and doses

- The local anesthetics most commonly used in the horse to induce regional anesthesia are 2% *lidocaine* HCl and 2% *mepivacaine* HCl.
  - *Mepivacaine* is longer acting than *lidocaine*, and it elicits a milder tissue reaction.
  - *Bupivacaine* HCl is longer acting than *mepivacaine* and is used when regional anesthesia is performed for relief of pain.

B. Deposition of local anesthetic

- When determining the site of pain causing lameness, the local anesthetic should be deposited accurately adjacent to the nerve.
  - This reduces the risk of inadvertently anesthetizing nearby nerves.
- The *smallest volume* that will anesthetize the nerve should be used.
  - A larger volume can be deposited when regional analgesia is used to provide analgesia for surgery or to provide temporary relief of pain.
  - The volume of local anesthetic used to anesthetize nerves located in the proximal portion of the limb is usually greater than that used to anesthetize nerves in the distal portion of the limb, because proximally located nerve trunks are thicker and located deeper, making accurate placement more difficult.
- Anesthesia of the nerves of the distal portion of the limb usually takes effect rapidly (5–10 min), but the larger nerves of the proximal portion of the limb may take 20 min or more to become anesthetized.

C. Equipment

- Needles and syringes should be disposable.
- Length and bore of the needle depend on the particular nerve to be anesthetized.

- Most nerves of the distal portion of the limb are anesthetized using a 25-gauge, 1.59 cm ($^5/_8$ inch) needle.
- Longer (e.g. 3.81 cm [1.5 inch]), larger-bore needles (e.g. 22- or 20-gauge) are used to anesthetize nerves located more proximally on the limb.
- If a relatively *large-bore* needle is to be used, subcutaneous deposition of a small amount of local anesthetic (using 25-gauge needle) may reduce resentment by the horse.
  - Syringes that lock on to the needle hub should *not* be used.
    - The syringe may have to be detached quickly from the needle to prevent the needle from being pulled out, bent, or broken.

III. Patient preparation

A. Physical restraint

- When regional anesthesia is used to determine the site of pain causing lameness, the horse should be restrained physically, rather than chemically, so that lameness can be evaluated without the influence of sedatives or analgesics.
- An experienced person should restrain the horse.
- Most horses can be controlled with a lip twitch.
- A fractious horse can be restrained in stocks to minimize risk to personnel, but stocks reduce accessibility of many sites of injection and may jeopardize the safety of some horses.
  - Anesthetizing nerves in the distal portion of the limb is usually easier for the clinician and safer for the horse when it is not restrained in stocks.

B. Chemical restraint

- Sedation may be necessary to control a fractious horse.
- *Xylazine* HCl (0.4 mg/kg, IV) or *acepromazine* (0.04 mg/kg, IV) can be administered without interfering significantly with assessment of gait.
- If there is concern that sedation may be detrimental to lameness evaluation, the horse can be examined after the effects of sedation dissipate, provided that the local anesthetic is longer lasting than the effects of the sedative.
  - Waiting until the effects of sedation dissipate may confound the results of regional anesthesia because the local anesthetic may diffuse and desensitize structures not intended to be desensitized.

C. Preparation of injection site

- Clipping the skin at the site of injection is not necessary, unless it aids palpation of landmarks used to determine the exact site of injection.
- The site of injection should receive a brief scrub, using an antiseptic soap.
  - If there is a risk of penetrating an adjacent synovial structure, the site should be more carefully prepared.
  - Sterile gloves are an unnecessary precaution against inducing infection, unless penetration of a synovial structure is a risk.

IV. General technique

- The clinician must have a good knowledge of landmarks surrounding the nerve to be desensitized.
- The more accurate the placement of the needle, the smaller the volume of local anesthetic required.

A. Needle insertion

- ○ The site of injection and preference of the clinician determine whether an injection is performed with the limb bearing weight or held.
- ○ The needle is inserted, without the syringe attached, with a quick thrust through the skin.
- ○ The needle is sometimes redirected, without being withdrawn through the skin, so that the anesthetic is deposited in several tissue planes.
- ○ If blood appears in the needle hub, the needle should be redirected slightly.

B. Localization of lameness

- ○ When localizing the site of pain causing lameness, regional anesthesia is usually initiated distally on the limb and advanced proximally, in a stepwise manner, until the lameness is eliminated.
- ○ If the site of pain causing lameness is quite far proximal, multiple perineural injections must be administered.
- ○ A *less common approach* is to first eliminate a large portion of the limb as the site of pain.
  - – This can be done on a rear limb, for example, by administering a low plantar block (i.e. a low, six-point block) to determine if the lameness is proximal or distal to the fetlock. If the horse remains lame, regional anesthesia below the fetlock joint is avoided, because it can be assumed that the site of pain causing lameness is proximal to the fetlock joint.
  - – This approach decreases the horse's discomfort and speeds the examination, providing that lameness is caused by pain proximal to the site of the initial regional block.
  - – This approach slows the lameness examination if the lameness is eliminated with the first regional block because the effects of the block must be allowed to dissipate before proceeding.

V. Checking for desensitization

- The effectiveness of anesthesia in desensitizing a particular region is usually determined by applying *noxious stimuli* to the skin overlying the region.
  - ○ Instruments used to apply *noxious* stimulation include ball-point pens, keys, or unfolded paper clips.
- Some horses react to stimulation of the distal portion of the limb by *striking*.
  - ○ Noxious stimulation may be applied more safely if the distal portion of the limb is held, or if stimulation is applied using a long, pointed instrument.

- The first assessment of skin sensation can usually be made at 5–10 min after regional anesthesia is administered to the *distal* portion of the limb.
  - The absence or presence of skin sensation usually provides a reasonable assessment of the efficacy of regional anesthesia.
  - Deep sensation may still be present, even though skin sensation is eliminated.
  - Conversely, deep sensation may sometimes be eliminated without the loss of skin sensation.
  - If the results are *inconclusive*, compare the horse's response to the same stimulation applied to the corresponding region of the *contralateral* limb.
    – A *stoic* horse may not react to noxious stimulation of skin, even when full sensation is retained.

VI. Complications

- Though rare, may include:
  - A broken needle becoming lodged in tissue.
  - Subcutaneous infection at the site of injection.
  - Infection of an inadvertently penetrated synovial structure.
  - Fracture displacement resulting from eliminating pain caused by a non-displaced fracture.
    – A horse should *not* receive regional anesthesia if a fracture is suspected.
  - Erroneous interpretation of the results resulting from:
    – Variations in neurological anatomy.
    – Inaccurate placement of the needle.

Comment: *The results of regional anesthesia should be interpreted with some degree of skepticism.*

VII. Fore limb: distal aspect

A. Palmar digital nerve block at the level of the cartilages of the foot

  - The neurovascular bundle containing the palmar digital nerve (PDN) can be palpated in the angle formed by the cartilage of the foot and the palmar aspect of the pastern (see Figs 16.1 and 16.2).
    – These nerves are usually anesthetized with the limb held.
  - To anesthetize each PDN, 1.5 ml or less of anesthetic are deposited at or distal to the proximal margin of the cartilage of the foot using a 25-gauge, 1.59 cm ($^5/_8$ inch) needle.
    – More proximal deposition might result in desensitization of the proximal interphalangeal joint.
  - Anesthesia of both PDNs at the level of the cartilages of the foot (i.e. distal to the dorsal branches of the PDNs) desensitizes the *entire* foot except for the dorsal part of the coronary band and the dorsal laminae of the foot (innervated by *dorsal branches* of the PDNs).
    – The dorsal branches of the palmar digital nerves do not innervate the distal interphalangeal joint, and so they need *not* be anesthetized to achieve complete analgesia of the distal interphalangeal joint.

Palmar nerve

Palmar digital nerve

Cartilage of the foot
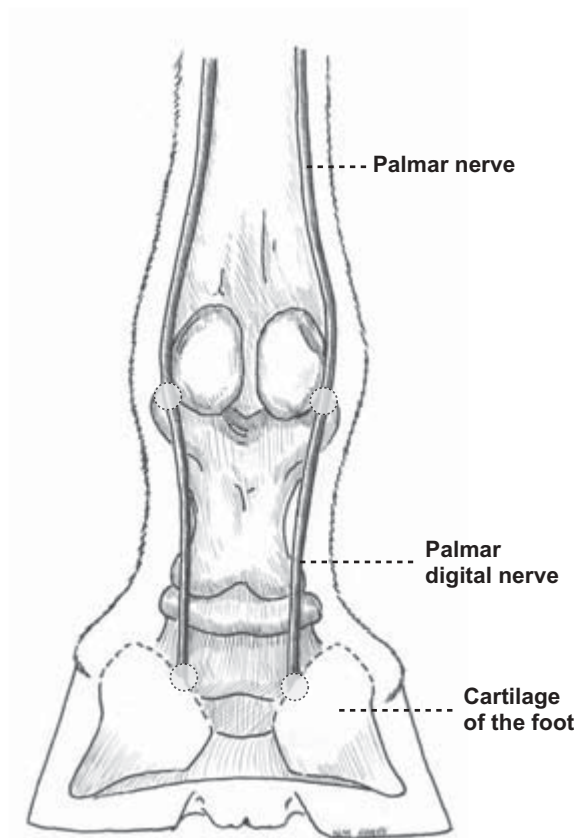
Fig. 16.1 Dorsopalmar view showing the site of perineural injection of the palmar digital nerves.

Palmar metacarpal nerve

Palmar nerve

Palmar digital nerve

Cartilage of the foot
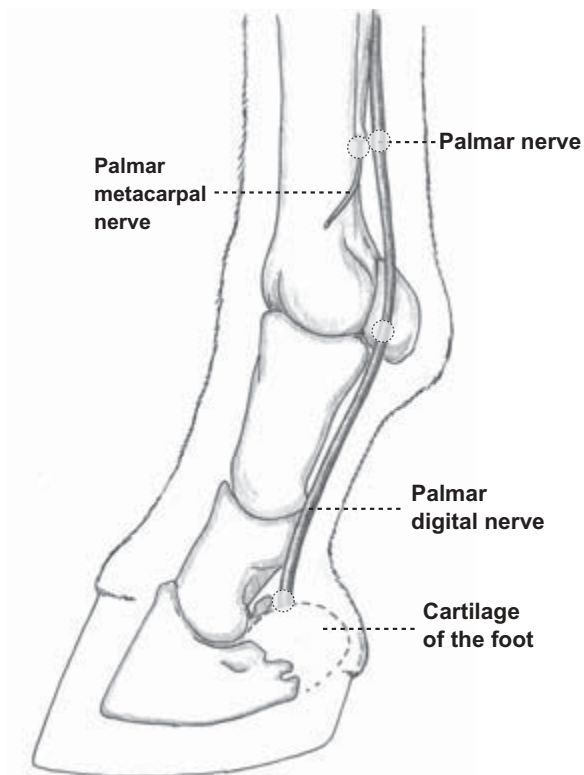
Fig. 16.2 Lateral view showing the site of perineural injection of the palmar digital nerves.

B. Midpastern ring block

- ○ Used by some clinicians if PDN block fails to improve lameness.
- ○ After the PDNs have been anesthetized (see above), 10 ml of local anesthetic are deposited subcutaneously around the dorsal half of the pastern, using a 25-gauge, 1.59 cm (^{5}/$_8$-inch) needle.
- ○ The dorsal branches of the PDNs contribute little to sensation within the foot and so a semi-ring block, performed after a PDN block has failed to improve lameness, is also unlikely to improve lameness.
- ○ Anesthesia of the PDNs will already have desensitized the entire foot with the exception of the dorsal part of the coronary band and the dorsal laminae.

C. Abaxial sesamoid nerve block

- ○ Used to localize the site of pain causing lameness that has not improved after anesthetizing the PDNs at the level of the ungular cartilages, or to desensitize the foot for *surgery*.
- ○ The neurovascular bundle containing the PDNs can be easily palpated along the abaxial border of each proximal sesamoid bone (see Figs 16.1 and 16.2).
- ○ The PDNs are anesthetized at this level using a 25-gauge, 1.59 cm (^{5}/$_8$-inch) needle.
- ○ The following will decrease the likelihood of partially desensitizing the metacarpophalangeal joint:
  - – Inserting the needle near the base of the proximal sesamoid bones.
  - – Using a small volume of local anesthetic (i.e. < 2 ml).
  - – Directing the needle distally, rather than proximally.
- ○ Anesthetizing the PDNs and their dorsal branches at the level of the proximal sesamoid bones (i.e. an abaxial sesamoid nerve block) desensitizes:
  - – The foot and the middle phalanx.
  - – The distopalmar aspects of the proximal phalanx and associated soft tissue.
  - – The proximal interphalangeal joint (occasionally).
  - – The palmar portion of the metacarpophalangeal joint (occasionally).

D. Low palmar nerve block (i.e. low four-point block)

- ○ With the low palmar nerve block (or low four-point block), the medial and lateral palmar and the medial and lateral palmar metacarpal nerves are anesthetized at the level of the distal end of the second and fourth metacarpal bones, *below the anastomotic branch* that connects the palmar nerves.
  - – This block is usually performed with the horse bearing weight on the limb.
- ○ The lateral and medial palmar nerves lie between the suspensory ligament and the deep digital flexor tendon.
  - – They are anesthetized by depositing local anesthetic (~ 2 ml) adjacent to the dorsal surface of the deep digital flexor tendon (25-gauge, 1.59-cm (^{5}/$_8$-inch) needle). (See Fig. 16.2.)
- ○ The lateral and medial palmar metacarpal nerves lie between the palmar surface of the third metacarpal bone and the axial surface of either the second or fourth metacarpal bone.
  - – They are anesthetized by depositing local anesthetic (1–2 ml) beneath the distal end of each small metacarpal bone, where the nerve emerges (25-gauge, 1.59 cm (^{5}/$_8$-inch) needle). (See Fig. 16.2.)

o   The low palmar nerve block is used to localize pain causing lameness that has not improved after anesthetizing the palmar digital nerves at the level of the base of the proximal sesamoid bones or to desensitize the foot or pastern for surgery.

o   Anesthetizing these four nerves desensitizes the *fetlock* and *distal structures*.

   –   Some skin sensation may remain over the dorsal aspect of the fetlock from sensory supply from a branch of the medial cutaneous antebrachial nerve.

E. High palmar nerve block (i.e. high four-point block)

o   The medial and lateral palmar and the medial and lateral palmar metacarpal nerves are anesthetized slightly below the carpometacarpal joint.

o   To anesthetize each *palmar* nerve in this location, 3–5 ml of local anesthetic are deposited through a needle [25-gauge, 1.59-cm (^{5}/8-inch)] inserted through heavy fascia to where the palmar nerve lies adjacent to the dorsal surface of the deep digital flexor tendon. (See Figs 16.3 and 16.4.)

   –   This is usually done with the horse *bearing weight* on the limb.

o   The lateral and medial *palmar metacarpal* nerves are anesthetized slightly below the carpometacarpal joint where each nerve lies between the palmar surface of the third metacarpal bone and the axial surface of the second or fourth metacarpal bone, by depositing local anesthetic (~ 5 ml) using a 20- to 22-gauge, 3.81 cm (1.5-inch) needle. (See Figs 16.3 and 16.4.)

   –   This is usually done with the limb held.

o   The high four-point block is sometimes the next block used to localize pain causing lameness that has not improved after anesthetizing the palmar and palmar metacarpal nerves at the level of the distal end of the second and fourth metacarpal bones.
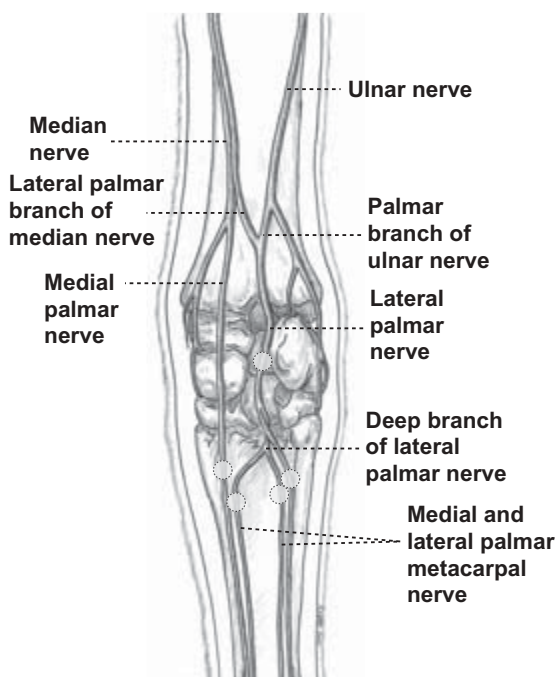
Fig. 16.3   Dorsopalmar view showing the sites of injection for the high palmar nerve block and the site for perineural injection of the lateral palmar nerve at the level of the accessory carpal bone.
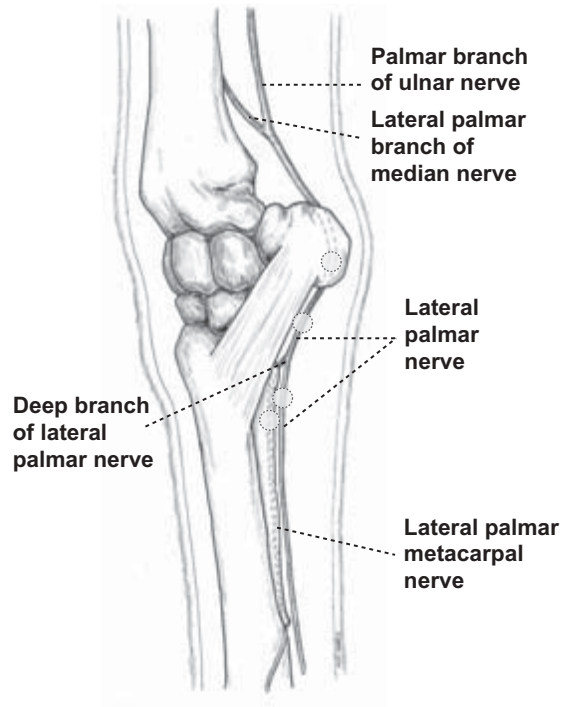
Fig. 16.4 Lateral view of the fore limb showing the sites of injection for the high palmar nerve block and the site for perineural injection of the lateral palmar nerve at the level of the accessory carpal bone.

- A *complication* of the high four-point block is anesthesia of the carpometacarpal and intercarpal joints from inadvertent penetration of a distopalmar outpouching of the carpometacarpal joint.

  Note: Direct infiltration of local anesthetic around the proximal aspect of the suspensory ligament to desensitize this structure also risks inadvertent anesthesia of the carpometacarpal and intercarpal joints.
- Anesthetizing the lateral and medial palmar nerves alone, slightly below the carpometacarpal joint, desensitizes the *flexor tendons*.
- Anesthetizing the palmar metacarpal nerves alone, at this level, desensitizes the small metacarpal bones and their interosseous ligaments, and all but the most proximal portion of the suspensory ligament.
- The inferior check ligament may *not* be desensitized with the high four-point block.

F. Lateral palmar nerve block

- The lateral palmar nerve originates proximal to the carpus and is formed by the *lateral palmar branch of the median* nerve and the *palmar branch of the ulnar* nerve.
- The lateral palmar nerve gives off its deep branch, which innervates the origin of the *suspensory* ligament and divides into the lateral and medial palmar metacarpal nerves, at the level of the proximal end of the third metacarpal bone.
- The lateral palmar nerve can be anesthetized at several sites.

Site 1

- o The origin of the suspensory ligament and the proximal end of the second and fourth metacarpal bones can be desensitized by anesthetizing the lateral palmar nerve at the level of the middle carpal joint, as it courses distal to the accessory carpal bone close to the accessoriometacarpal ligament, before it gives off a deep branch that innervates these structures.
- o The *site of injection* is located on the palmar border of the accessoriometacarpal ligament, midway between the ligament's origin on the distal aspect of the accessory carpal bone and its insertion on the proximal aspect of the fourth metacarpal bone. (See Fig. 16.4.)
- o 5 ml of local anesthetic are deposited beneath the 2–3 mm thick flexor carpal retinaculum using a 20- to 22-gauge, 2.54 cm (1-inch) needle.
  - – This is usually done with the horse *bearing weight* on the limb.
- o This technique results in a high incidence of *penetration of the carpal synovial sheath*, and so could lead to erroneous conclusions if the amount of local anesthetic deposited within the carpal synovial sheath were enough to ameliorate pain associated with disease of the structures contained within this *synovial* cavity.
- o Although the site of injection is close to the distal aspect of the carpus, inadvertent infiltration of local anesthetic into the carpometacarpal and intercarpal joints using this technique is unlikely.

Site 2

- o The lateral palmar nerve can also be anesthetized at the medial aspect of the *accessory carpal bone*. (See Figs 16.3 and 16.4.)
- o At this level, the lateral palmar nerve lies adjacent to the medial aspect of the accessory carpal bone, together with the lateral palmar vein and artery.
- o The site of injection is palpated as a longitudinal groove in the fascia over the medial aspect of the accessory carpal bone, dorsal to the insertion of the flexor retinaculum that forms the palmaromedial aspect of the carpal canal.
  - – This is done with the horse *bearing weight* on the limb.
- o A 25-gauge, 1.59 cm (^{5}/8-inch) needle is inserted into the distal third of the groove in a mediolateral direction, and when the point of the needle contacts the medial aspect of the accessory carpal bone 1.5–2 ml of local anesthetic are injected.
- o This technique of anesthetizing the lateral palmar nerve *avoids* inadvertent deposition of the local anesthetic into the *carpal synovial sheath*.
- o Amelioration of lameness after anesthesia of the lateral palmar nerve alone, proximal to its deep branch, incriminates the proximal portion of the suspensory ligament or the proximopalmar metacarpal area as the site of pain causing lameness, provided that sites distal to these structures have been eliminated.
- o Anesthetizing the medial palmar nerve in conjunction with anesthesia of the lateral palmar nerve at the level of the proximal aspect of the metacarpus provides extensive desensitisation of the distal portion of the limb (i.e. metacarpus and below).

VIII. Fore limb: proximal aspect

- The carpus and distal aspect of the limb can be desensitized by anesthetizing the median, ulnar, and medial cutaneous antebrachial nerves.

● Although these nerves are sometimes anesthetized for diagnostic purposes, they are most commonly anesthetized to desensitize the distal portion of the limb for surgery.

A. Median nerve

○ The median nerve is anesthetized on the caudomedial aspect of the radius, just below the elbow joint, where the ventral edge of the posterior superficial pectoral muscle inserts on the radius (see Fig. 16.5.).

○ A 20-gauge, 5.08–6.35 cm (2–2.5 inch) needle is inserted at this site and angled proximally and laterally through the fascia close to the caudal surface of the radius to a depth of 2.5–4 cm, and ~ 10 ml of local anesthetic are deposited.

   – The needle is advanced close to the radius to avoid the median vein and artery.

○ Anesthesia of the median nerve alone *partially* desensitizes the carpus and distal aspect of the antebrachium and the structures innervated by the medial and lateral palmar nerves.

B. Ulnar nerve

○ The ulnar nerve is anesthetized about 10 cm above the accessory carpal bone, at which point it lies about 0.5–1 cm below the skin surface, under the superficial fascia, in the groove between the ulnaris lateralis and flexor carpi ulnaris muscles.
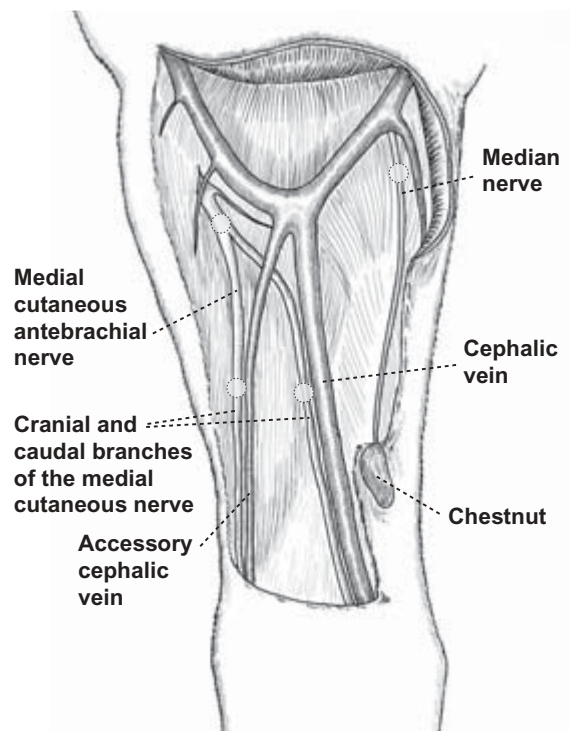
Fig. 16.5 Medial aspect of the antebrachium showing the site of perineural injection of the median nerve and the sites of perineural injection of the cranial and caudal branches of the medial cutaneous nerve.

o   ~ 10 ml of local anesthetic are infused superficially and deeply, through a 20-gauge, 3.81 cm (1.5 inch) needle.

o   Anesthetizing the ulnar nerve desensitizes the skin of the lateral aspect of the forelimb distal to the injection site down to the fetlock.

o   Lameness caused by lesions of the accessory carpal bone and surrounding structures, the small metacarpal bones and their interosseous ligaments, and the suspensory ligament may be *partly* ameliorated by anesthetizing the ulnar nerve.

C. Medial cutaneous antebrachial nerve

o   Anesthesia of the medial cutaneous antebrachial nerve, a branch of the musculocutaneous nerve, desensitizes skin on the dorsal and medial aspects of the metacarpus.

o   The medial cutaneous antebrachial nerve can be anesthetized immediately above the dorsal aspect of the elbow joint where it can be palpated as it crosses the *lacertus fibrosus*.

o   Distal to the lacertus fibrosus, on the medial aspect of the forelimb, the medial cutaneous antebrachial nerve forms two branches, which can be blocked on the medial aspect of the radius, halfway between the elbow and the carpus (i.e. about 10 cm proximal to the chestnut). (See Fig. 16.5.)

–   One branch lies on the cranial aspect of the cephalic vein, and the other branch lies on the cranial aspect of the accessory cephalic vein.

–   Because the location of these branches varies, local anesthetic should be infiltrated subcutaneously, cranial and caudal to the cephalic and accessory cephalic veins.

–   5 ml of anesthetic are infiltrated at each site.

IX. Rear limb

A. Plantar digital nerve block at the level of the cartilages of the foot

o   The technique of anesthetizing the plantar digital nerves is identical to that of anesthetizing the palmar digital nerves. (See Figs 16.1 and 16.2.)

o   Anesthesia of both plantar digital nerves at the level of the cartilages of the foot desensitizes the entire foot, except for the dorsal part of the coronary band and the dorsal laminae of the foot which are innervated by the lateral and medial dorsal metatarsal nerves (branches of the deep peroneal nerve).

o   The lateral and medial dorsal metatarsal nerves course distally along either side of the long digital extensor tendon into the laminar corium of the foot.

o   The incidence of lameness caused by disease in the rear foot is much lower than that of the fore foot, and the likelihood of ameliorating lameness with this block is small.

B. Midpastern ring block

o   The midpastern ring block of the rear limb is performed in the same way as the midpastern ring block of the fore limb.

–   As for the fore limb, there is *little indication* for performing this block.

C. Abaxial sesamoid nerve blocks

o The plantar abaxial sesamoid nerve block desensitizes the same structures that are desensitized with the *palmar* abaxial sesamoid nerve block.

o The technique of the *plantar* abaxial sesamoid nerve block at the level of the proximal sesamoid bones is identical to that of the palmar abaxial sesamoid nerve block. (See Figs 16.1 and 16.2.)

o The likelihood of ameliorating lameness with the abaxial sesamoid nerve block in a rear limb is *much lower* than with the same block in the forelimb.

D. Low plantar nerve block (i.e. the low six-point nerve block)

o For the low plantar nerve block, the medial and lateral plantar nerves, the medial and lateral plantar metatarsal nerves, and the dorsal metatarsal nerves are anesthetized at the level of the distal end of the second and fourth metatarsal bones, below the anastomotic branch that connects the plantar nerves. (See Figs 16.1 and 16.2.)
   – These are usually anesthetized with the horse *bearing weight* on the limb.

o The *lateral and medial plantar nerves* lie between the suspensory ligament and the deep digital flexor tendon, and each is anesthetized by depositing ~ 2 ml of local anesthetic adjacent to the dorsolateral or dorsomedial aspect of the surface of the deep digital flexor tendon, using a 25-gauge, 1.59 cm ($^5/_8$ inch) needle.

o The *lateral and medial plantar metatarsal nerves* are anesthetized by depositing local anesthetic (1–2 ml), beneath the distal end of each small metatarsal bone, where the nerves emerge, using a 25-gauge, 1.59 cm ($^5/_8$ inch) needle.

o The *lateral and medial dorsal metatarsal nerves* are anesthetized by depositing 2 ml of local anesthetic on each side of the long digital extensor tendon at the same level.

o The *low plantar nerve* block desensitizes the fetlock and structures distal to it.

o Because of the *low incidence* of lameness caused by pain at or below the rear fetlock, the low plantar block is sometimes used to rule out lameness in the fetlock region and below, before proceeding with diagnostic regional or intra-articular anesthesia to desensitize areas of the rear limb more likely to be the site of pain causing lameness.

E. High plantar nerve block (i.e. the high six-point nerve block)

o Anesthesia of the medial and lateral plantar nerves, the medial and lateral plantar metatarsal nerves, and the medial and lateral dorsal metatarsal nerves just distal to the tarsometatarsal joint provides complete analgesia to the distal portion of the limb (i.e. metatarsus and below).

o To anesthetize the plantar metatarsal nerves just distal to the tarsometatarsal joint, a 22- or 20-gauge, 3.81 cm (1.5 inch) needle is inserted about 1 cm distal to the tarsometatarsal joint and axial to the second or fourth metatarsal bone, until its point contacts the third metatarsal bone. Five milliliters of local anesthetic are deposited at this location. (See Fig. 16.6.)
   – This is usually done with the horse *bearing weight* on the limb.
   – Anesthetizing both plantar metatarsal nerves alone, just distal to the tarsometatarsal joint, desensitizes the small metatarsal bones and their interosseous ligaments, and all but the most proximal portion of the suspensory ligament.

- – Although unlikely, local anesthetic could be *inadvertently* placed in the tarso-metatarsal joint with this block.
  - – Inadvertent administration of local anesthetic into the tarsal sheath, however, *is likely* when performing a high plantar block.
- o To anesthetize the medial and lateral plantar nerves just distal to the tarsometatarsal joint, 3–5 ml of local anesthetic are deposited using a 25-gauge, 1.59 cm ($^5/_8$ inch) needle inserted through *heavy fascia* to where each plantar nerve lies adjacent to the dorsal surface of the deep digital flexor tendon. (See Fig. 16.6.)
  - – This is usually done with the horse bearing weight on the limb.
  - – Anesthetizing the lateral plantar nerve at this level anesthetizes its deep branch, which divides into the medial and lateral plantar metatarsal nerves.
  - – Anesthesia of the lateral plantar nerve alone at this level, desensitizes the same structures that are desensitized by anesthesia of the medial and lateral plantar metatarsal nerves.
- o All but the proximodorsal aspect of the limb distal to the tarsometatarsal joint is desensitized by anesthetising the medial and lateral plantar and plantar metatarsal nerves.
- o Subcutaneous deposition of local anesthetic at the dorsomedial and dorsolateral aspect of the metatarsus at this level anesthetizes the dorsal metatarsal nerves and completes the high plantar nerve block. (See Fig. 16.6.)

Superficial peroneal nerve

Lateral plantar nerve

Deep branch of lateral plantar nerve

Lateral plantar metatarsal nerve
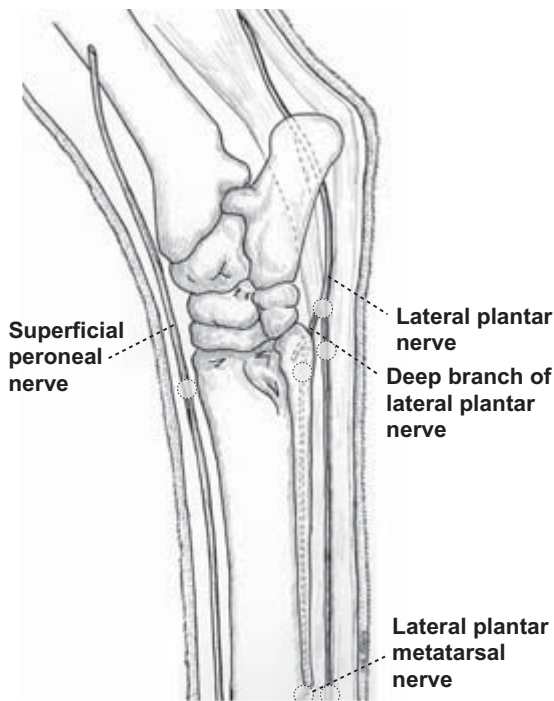
Fig. 16.6   Lateral view of the rear limb showing the sites of injection for the high palmar nerve block.
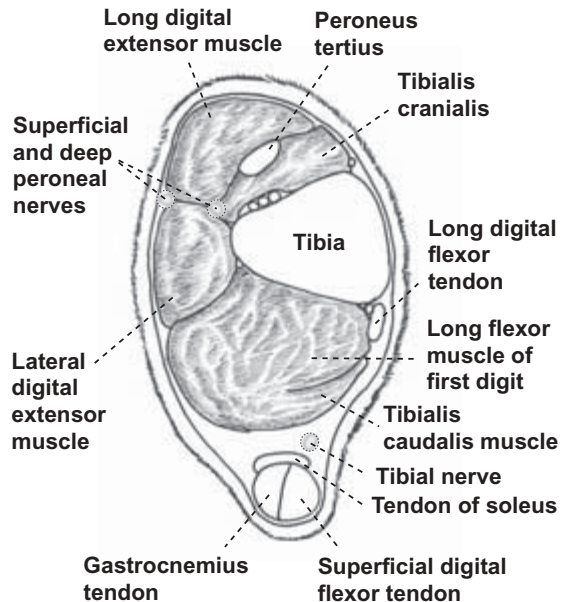
Fig. 16.7   Cross-section of tibia approximately 10 cm proximal to the point of the hock showing the tibial and superficial and deep peroneal nerves.

F. Tibial and peroneal (fibular) nerve blocks

Tibial nerve

- o The tibial nerve is anesthetized approximately 10 cm above the point of the hock on the *medial* aspect of the limb where the nerve can be palpated on the caudal surface of the tibialis caudalis muscle, cranial to the Achilles tendon. (See Fig. 16.7.)
    - – The neurovascular bundle containing the nerve is most easily palpated at this level *while the limb is flexed*.
- o To anesthetize the *tibial* nerve, local anesthetic (15–25 ml) is deposited at this site, in several planes, in the fascia that overlies the tibialis caudalis muscle, through a 20- or 22-gauge, 3.81 cm (1.5 inch) needle.
- o Amelioration of lameness after the tibial nerve has been anesthetized incriminates the *suspensory ligament* or the proximoplantar metatarsal area as the site of pain, provided that more distal structures of the limb have been eliminated as a source of pain using a low plantar nerve block.

G. Deep and superficial peroneal nerves

- o To completely desensitize the hock and the portion of limb distal to the hock, the tibial nerve and the deep and superficial peroneal (fibular) nerves must be anesthetized.
- o The *peroneal* nerves are usually anesthetized on the lateral aspect of the limb, about 10 cm above the point of the hock, in the groove formed by the lateral and long digital extensor muscles. (See Figs 16.7 and 16.8.)
- o To anesthetize the deep peroneal nerve, a 20- to 22-gauge, 3.81–5.08 cm (1.5–2 inch) needle is inserted into the groove and directed slightly caudally until it contacts the caudal aspect of the tibia.
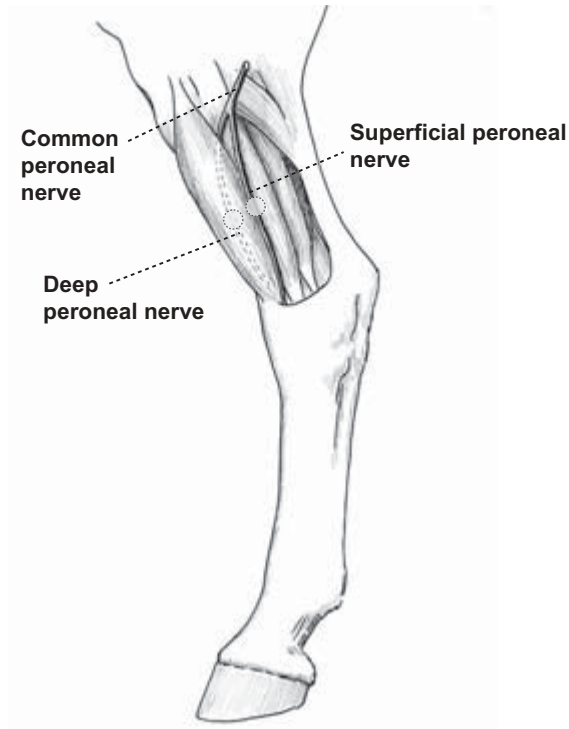
Fig. 16.8   Lateral view of the rear limb showing the sites of injection of the deep and superficial peroneal nerves.

- o After depositing local anesthetic (10–15 ml) at this site to anesthetize the *deep* peroneal nerve, more local anesthetic (10–15 ml) is deposited superficially in three or four planes to anesthetize the *superficial* peroneal nerve, as the needle is withdrawn.
- o Anesthetizing the tibial and the deep and superficial peroneal nerves above the point of the hock desensitizes the entire distal portion of the limb.
- o The horse may *drag the toe* of the desensitized limb when the tibial and superficial and deep peroneal nerves are anesthetized.

17   Epidural analgesia and anesthesia

- The use of the epidural route for injection of drugs that result in analgesia and/or anesthesia of the perineal area has become more common in the horse.
- Epidural injection is an effective method of providing clinical effects (analgesia and/or anesthesia).
  - Depending on the drug and dose used, these effects may also affect more rostral areas.
- The epidural space is accessible at the lumbosacral (LS) joint (cranial epidural) and caudal to the sacrum (caudal epidural).
- *Caudal epidural (sacrococcygeal or C1–C2 space)* is the preferred and most commonly used technique in the horse as it is easier and safer to perform.
  - No risk of dural puncture and CSF tap.
  - Less risk of motor blockade and ataxia.
    - However, a large volume of injectate can cause the drug to move forward and result in a cranial epidural block.
    - This will also occur with a catheter advanced rostrally towards the lumbosacral area.
    - This rostral spread may be beneficial or detrimental depending on the drug and the goal in question (see specific drugs below).
- *Cranial epidural (lumbosacral space)* is less commonly used.
  - Technically more difficult to perform, especially in heavily muscled horses.
    - Requires longer needles.
    - Landmarks are not so obvious.
  - Can result in dural puncture and CSF tap.
    - A paramedian needle approach and a 5–10° angle decrease the risk of dural puncture.
  - Higher risk of motor blockade and ataxia.
  - A catheter advanced *caudally* from the LS space to the sacral area can produce a caudal epidural block.
  - A catheter advanced *rostrally* from the LS space to the thoracolumbar area can provide segmental analgesia.

I. Anatomy and technique for caudal epidural (see Fig. 17.1)

A. Location

- The spinal cord extends to the level of the caudal half of the second sacral vertebra.
- Epidural injection can be performed at the sacrococcygeal (SC) or first intercoccygeal (C1–C2) space, without risk of spinal injection.
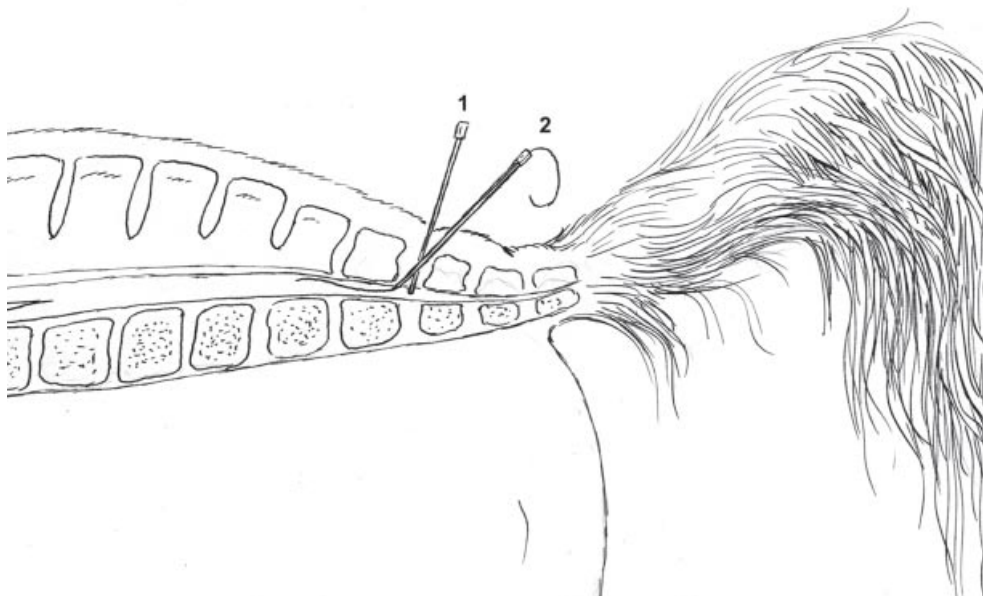
Fig. 17.1   Schematic representation of caudal epidural. (1) Hypodermic needle inserted between C1 and C2. (2) Catheter placement through Tuohy needle.

- o Either space is located by moving the tail up and down while palpating the intervertebral space.
  - – As a guide, the spaces are approximately 1–3 inches (2.5–7.5 cm) cranial to the start of the tail hairs.
  - – The depth of the space from the skin is 1.3–3 inches (3.5–8 cm).

B. Technique

- o Aseptic technique is mandatory.
- o Superficial local anesthetic infiltration (1 ml of *lidocaine*, 22-gauge needle) at the site of injection is optional to facilitate insertion of the needle or catheter.
- o Sedation may be necessary in the awake horse.
- o Over-sedation should be avoided as the horse won't then stand squarely, making it more difficult to keep on the midline when inserting the needle/catheter.
- o Needles, spinal needles, or epidural catheters can be used.
  - – 22-, 20-, or 18-gauge, 1.5–3.5 inch needle or spinal needle, depending on the size of the horse.
  - – 17- or 18-gauge, 3–3½ inch Tuohy needle for insertion of a 19 or 20-gauge epidural catheter.
- o Needles and spinal needles are recommended for *one-time* drug administration.
- o Catheters are recommended for *repeated* drug administration and *long-term* use.
- o The needle is introduced at a 30–90° angle to the plane of the skin and advanced into the epidural space by traversing the intervertebral ligament.

o   Volume of injection can be increased with preservative-free 0.9% saline.
  – Volumes <10 ml can be injected in less than a minute.
  – Volumes >10 ml should be injected slowly (5–10 min), due to mechanical compression of nerve endings in the epidural space resulting in the horse becoming recumbent.

C. Verification of needle or catheter placement

o   Placement is verified by one or more of the following methods:
  – Hanging-drop technique: aspiration of a drop of fluid from the hub of the needle by the negative pressure of the epidural space.
  – Lack of resistance upon injection of air.
  – Lack of resistance upon injection of drugs.
  – Ease of advancement of epidural catheter.
  – Clinical effects (tail becomes relaxed).
o   *Catheters* are introduced 10–30 cm into the epidural space.
  – Should be secured to the skin with adhesive and suture material.
  – Asepsis should be maintained.
  – Epidural catheters can remain in place for weeks.

II. Indications for epidural drug administration

• Depending on the drug(s), epidural techniques can provide effects that range from analgesia to complete anesthesia. Therefore, indications include:
  o   Anesthesia of the standing horse for surgery of the rectum, anus, perineum, tail, urethra, bladder, vulva or vagina.
  o   Adjunct analgesia during general anesthesia for surgery of these same anatomical areas and hind limbs.
  o   Postoperative pain management of these same anatomical areas and hind limbs.
  o   *Xylazine* is the only drug with reported analgesic effects in more rostral anatomical areas (e.g. fore limb) after epidural administration.

III. Contraindications

• Skin infection near the site of injection.
• Spinal cord disease.
• Weak patients with an increased risk of ataxia/recumbency.

IV. Effects

A. Analgesia

o   Is induced by drugs that block conduction in Aδ and/or C fibers.
  – Local anesthetics and α_2 agonists block both types of fiber.
  – Opioids (more selective for C fibers).

B. Anesthesia

- ○ Is induced by drugs that block Aδ and C fibers.
  - – Local anesthetics, α_2 agonists, *ketamine*.

C. Other spinal effects

- ○ *Proprioceptive deficits* are caused by drugs that block Aβ fibers.
  - – Local anesthetics and *xylazine*.
- ○ *Motor blockade* (e.g. ataxia, recumbency) is caused by drugs that block A-motor fibers.
  - – Local anesthetics and α_2 agonists (high doses).
- ○ *Sympathetic blockade* is caused by drugs that block β fibers.
  - – Local anesthetics only.

D. Systemic effects

- ○ Absorption of the drug by epidural vessels can result in different systemic effects depending on the drug injected.
  - – Sedation (e.g. α_2 agonists).
  - – Excitement (e.g. opioids).
  - – Ataxia (e.g. local anesthetics).
  - – Cardiorespiratory effects including hypotension, hypertension, bradycardia can result from α_2 agonist administration.

V. Complications

- Failure to achieve analgesia and/or anesthesia can result from poor technique, previous epidurals (development of fibrous tissue at the site), or anatomical anomalies.
- Excessive ataxia and occasionally recumbency from overdose of local anesthetics, α_2 agonists or the combination.
  - ○ Ataxia and weakness may not be evident while the horse is standing in the stocks, so it is important to evaluate the horse before attempting to move it.
  - ○ If recumbency results, sedation may be necessary to maintain the horse in this position until motor function is regained.
    - – If necessary, the horse may be transported to a recovery stall under light, general anesthesia until recovery of motor function.
- Sedation and cardiovascular depression associated with systemic absorption of the drug.
- Hindlimb ataxia and general discomfort from injecting a large volume or injecting too rapidly.
- A case of severe systemic pruritus has been reported following epidural coadministration of *morphine* and *detomidine*.

VI. Drugs

A. Local anesthetics

- ○ Epidural local anesthetics can induce dose-related sensory, motor, and sympathetic blockade.
- ○ Main indication is to produce perineal anesthesia for surgical procedures.
- ○ Higher doses can travel rostrally and block all fiber types, causing ataxia/paresis and hypotension.
- ○ Can be combined with α_2 agonists (see Section F – Combinations, below).

Lidocaine (2%) or mepivacaine (2%)
- ○ The most commonly used local anesthetic for epidurals.
- ○ Dose: 0.2–0.25 mg/kg (1–1.25 ml of 2% *lidocaine* or *mepivacaine*/100 kg).
  - – Volume of injection can be increased with preservative-free 0.9% saline, but should not exceed 10 ml (500 kg horse), to avoid rostral spread and adverse effects.
- ○ Fast onset of complete analgesia (6–10 min) and relatively short duration of action (45–60 min).

Ropivacaine (0.5%)
- ○ Longer acting than *lidocaine*.
- ○ Dose: 0.8 mg/kg (1.6 ml of 0.5% *ropivacaine*/100 kg).
  - – Volume of injection can be increased with preservative-free 0.9% saline, but should not exceed 10 ml (500 kg horse) to avoid rostral spread and adverse effects.
- ○ Fast onset of complete analgesia (10 min) and intermediate duration of action (3 hours).
- ○ Minimal ataxia and cardiorespiratory effects.

B. Opioids

- ○ A lower dose (than that used systemically) can be given epidurally and results in prolonged analgesic effects.
  - – Proximity of drug deposition to the spinal cord facilitates the interaction with opioid receptors.
- ○ Epidural opioids result in analgesia, but *not* anesthesia.
- ○ Main indication is to produce intra- and postoperative analgesia of the perineal area and hind limb.
  - – Effects on abdominal pain have not been established.
- ○ *Morphine* and *methadone* are the most effective opioids for epidural injection.
  - – Other opioids have proven less effective and are not recommended.

Morphine (0.1–0.2 mg/kg)
- ○ Has a slow onset (1–5 hours) and long duration (6–16 hours) of action.
- ○ Mild systemic opioid effects can be apparent in the awake horse.
- ○ Reduces MAC of *halothane* for hindlimb stimuli by 14%.
  - – A more profound MAC reduction may result if *morphine* is administered a few hours prior to surgery.

- o The volume of injection can be increased to a maximum of 20–30 ml in a 450 kg horse, to facilitate rostral spread of *morphine* over the spinal cord.
  - – Preservative-free 0.9% saline should be used as a diluent.
- o Preservative-containing *morphine* solutions are more concentrated (10 or 15 mg/ml) than preservative-free (1 mg/ml).
  - – Dilution of preservative-containing solutions with preservative-free 0.9% saline decreases the risk of neurotoxicity from preservatives.
  - – A large volume of preservative-free morphine must be injected slowly (15 min) to avoid compression of nerve endings.
  - – Preservative-containing solutions are more practical and less expensive than preservative-free solutions.

Methadone (0.1 mg/kg)
- o Rapid onset (15 min) and intermediate duration (5 hours) of action.
- o Preservative-free solution is 1% (10 mg/ml) and should be diluted with preservative-free 0.9% saline to a maximum of 20–30 ml in a 450 kg horse.

C. Tramadol

- o At a dose of 1 mg/kg, *tramadol* has a rapid onset (≤ 30 min) and an intermediate duration (4–5 hours) of action of complete analgesia.
- o Injection should be diluted to a maximum volume of 20–30 ml (in a 450 kg horse) with preservative-free 0.9% saline.

D. Alpha$_2$ agonists

- o Epidural administration provides analgesia of longer duration than systemic doses.
- o Main indications are to provide intra- and postoperative analgesia of the perineum.
- o High doses can block all types of fiber, causing ataxia/paresis.
  - – Do not give a complete sensory block at clinical doses.
- o Systemic effects (sedation, hypertension/hypotension, bradycardia) are common.
- o *Xylazine* and *detomidine* are most commonly used.

Xylazine (0.17–0.22 mg/kg)
- o Intermediate onset of complete analgesia (15–30 min) and an intermediate duration of action (3.5 h).
- o Surgical analgesia of the perineal area, hind limb, and fore limb.
- o Reduces MAC of *halothane* in a segmental manner both in the fore and hind limb, by 34% and 43% respectively.
- o Volume of injection in a 450 kg horse:
  - – May be diluted to a maximum of 10 ml for perineal analgesic/anesthetic effects.
  - – May be diluted to a maximum of 20–30 ml if rostral spread is desired for analgesic effects.

Detomidine (0.01–0.06 mg/kg)
- o Intermediate onset of analgesia (10–25 min) and intermediate duration of action (2 hours).

○ Combining with *morphine* (0.1–0.2 mg/kg) is recommended for intra- and post-operative pain, as well as long-term management of traumatic hindlimb accidents.
○ Volume of injection may be diluted to a maximum of 10 ml (in a 450 kg horse) to limit rostral spread and side effects.

E. Ketamine

○ Epidural *ketamine* blocks NMDA receptors in the spinal cord.
○ Causes analgesia of the tail, perineum, and upper hind limb.
○ Fast onset of analgesic action (10 min) and a short duration of action (30–75 min) are dose-dependent (0.5–2 mg/kg).
○ Systemic effects (e.g. sedation, ataxia) can occur with high doses.
○ Reduces MAC of *halothane* in the hind limb by 13–17%.
○ Epidural injection should be diluted (10–30 ml in a 450 kg horse).

F. Combinations

Opioids and α_2 agonists
○ *Morphine* can be combined with α_2 agonists.
  – This provides a faster onset from the α_2 drugs, as well as giving the prolonged effect of morphine.
○ The full dose of each drug may be given without adverse effects.
○ Useful for long-term pain management.

Alpha$_2$ agonists and local anesthetics
○ When used in combination, careful dosing of the local anesthetic is required to avoid excessive ataxia from an additive effect.
  – Dose of local anesthetic should be decreased by 30%.
○ Useful for standing surgery.
○ Prolonged effect over local anesthetic alone.

18 Anesthesia of the head and penis

Jim Schumacher

Anesthesia of the head

- Nerve blocks of the head region, apart from those of the eye, are most commonly performed to facilitate dental surgeries.
- However, certain blocks can be used in the sedated horse to allow suturing of soft tissue wounds of the head.
- Blocks are shown in Fig. 18.1.

A. Infraorbital nerve block

- ○ Facilitates surgery of the *nasal area* or *incisors*.
- ○ *Adequate restraint* and *great care* should be taken during its administration, because the block is poorly tolerated by the horse.
- ○ The infraorbital nerve can be anesthetized at its point of emergence from the *infraorbital foramen* or within the foramen.
  - – If anesthetized at its *point of emergence*, the desensitized area comprises the skin of the lip, nostril, and face on that side of the head, up to the level of the foramen.
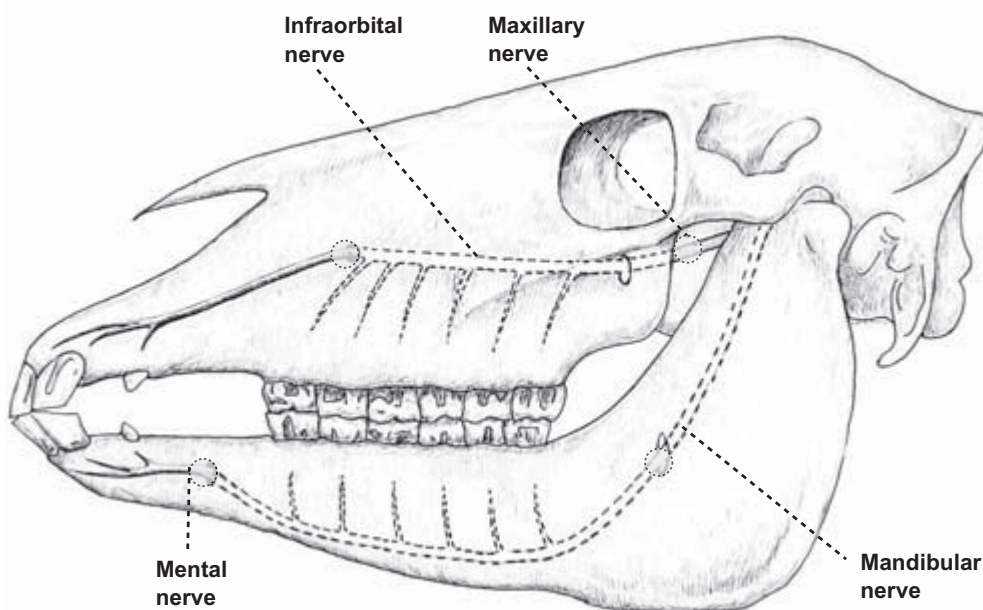
Fig. 18.1 Anatomical locations for nerve blocks of the head.

   – If anesthetized *within the infraorbital canal*, additional desensitized structures
     include the ipsilateral canine tooth, wolf tooth, second and third premolars, pre-
     maxillary incisor teeth, and associated alveoli and gingiva.

Location
   o The infraorbital foramen is located by placing a thumb in the notch formed by the
     nasal bone and premaxillae, and the middle finger on the rostral end of the facial crest.
   o The foramen is located with the index finger halfway between and 1–3 cm caudal to
     an imaginary line between these points.
   o The bony ridge of the foramen can be palpated beneath the ventral edge of the levator
     nasolabialis muscle.

Technique (within the infraorbital canal)
   o Insert a 21- or 22-gauge, 5 cm needle through the skin 2 cm rostral to the foramen
     after pushing the ventral edge of the levator nasolabialis muscle dorsally.
   o Insert the point of the needle about 2.5 cm into the canal, and deposit 4–5 ml of local
     anesthetic.

B. Maxillary nerve block

   o All the dental structures of the *maxilla* and *premaxilla*, as well as the *paranasal
     sinuses* and *nasal cavity*, can be desensitized.

Location
   o The maxillary nerve at the pterygopalatine fossa, where the nerve enters the infraorbital
     canal to become the infraorbital nerve.

Technique
   o Insert the point of a 20- to 22-gauge, 8.9 cm (3.5 inch) spinal needle just ventral to
     the zygomatic process and dorsal to the transverse facial vessels at the level of the
     caudal third of the eye.
       – The needle should have a short bevel to avoid venepuncture.
   o The point of the needle is inserted at a 90° angle to the head so that it enters the
     pterygopalatine fossa just caudal to the maxillary tuberosity at a depth of approxi-
     mately 5.0–6.5 cm.
       – The horse may jerk its head, indicating that the needle has contacted the nerve.
       – If blood is withdrawn from the needle, the needle has been inserted too far
         ventrally or caudally.
   o 15–20 ml of local anesthetic should be deposited near the pterygopalatine fossa as
     the needle is withdrawn slightly.
   o Structures innervated by the maxillary nerve are desensitized within 10–15 min.

C. Mandibular nerve block

   o Desensitizes one side of the *mandible* and all its dental structures.
   o The mandibular nerve can be anesthetized where it enters the mandibular canal at the
     mandibular foramen to become the mandibular alveolar nerve.

Location
- o The mandibular foramen is located on the medial aspect of the vertical ramus of the mandible, at the intersection of an imaginary line that extends along and caudal to the occlusal surface of the mandibular cheek teeth and a second imaginary line that passes perpendicular to the first line from the lateral canthus of the eye.

Technique 1
- o Insert the point of a 20- to 22-gauge, 15.24 cm (6 inch) spinal needle at the ventral border of the ramus, just rostral to the angle of the mandible.
- o Advance the point of the needle vertically for 10–15 cm along the medial surface of the ramus to reach the intersection of the previously described imaginary lines, and deposit 15–20 ml of local anesthetic.
- o Structures innervated by the mandibular nerve are desensitized within 15–30 min.

Technique 2
- o Insert the point of a 20- to 22-gauge, 15.24 cm (6 inch) spinal needle at the caudal border of the vertical ramus of the mandible about 3 cm below the temporomandibular articulation, in the depression between the wing of the atlas and the base of the ear.
- o Advance the point of the needle rostrally along the medial surface of the ramus following the path of the imaginary horizontal line that extends caudally from the occlusal surface of the mandibular cheek teeth.
- o Advance to the mandibular foramen located at the intersection of the previously described imaginary lines, keeping the point as close as possible to the medial surface of the mandible, and deposit 15–20 ml of local anesthetic.
- o Structures innervated by the mandibular nerve are desensitized within 15–30 min.

D. Mental nerve block

- o The mandibular alveolar nerve traverses the mandibular canal and emerges at the mental foramen, and at this point it is termed the mental nerve.
- o Anesthetizing the mandibular alveolar nerve at the *mental foramen* or within the rostral end of the *mandibular canal* is referred to as the *mental nerve block*.
  - – Anesthetizing the mental nerve *as it exits the mental foramen* desensitizes the skin of the lip and chin of that side of the head.
  - – Anesthetizing the mental nerve *within the mandibular canal* desensitizes the mandibular canine, incisors, and cheek teeth and associated alveoli and gingiva.

Location
- o The mental foramen is located on the lateral aspect of the horizontal ramus of the mandible in the intermandibular space below the commissure of the lips.
- o The bony ridge of the mental foramen can be palpated by pushing the tendon of the depressor labii inferioris muscle dorsally.

Technique (within the mandibular canal)

- o   Insert a 21- or 22-gauge, 3.81 cm (1.5 inch) needle through the skin 2 cm rostral to the mental foramen after pushing the tendon of the depressor labii inferioris muscle dorsally.
- o   Advance into the mandibular canal as far as possible, and deposit 5–10 ml of local anesthetic.

Anesthesia of the penis and pudendal region

- ●   Blocking the pudendal nerves at the ischium desensitizes the penis and internal lamina of the prepuce.
- ●   The penis then relaxes and can be extruded.

A. Location (see Fig. 18.2)

- o   The sites of injection are on the right and left sides of the anus, about 2 cm dorsal to the ischial arch and an equal distance lateral to the anus.
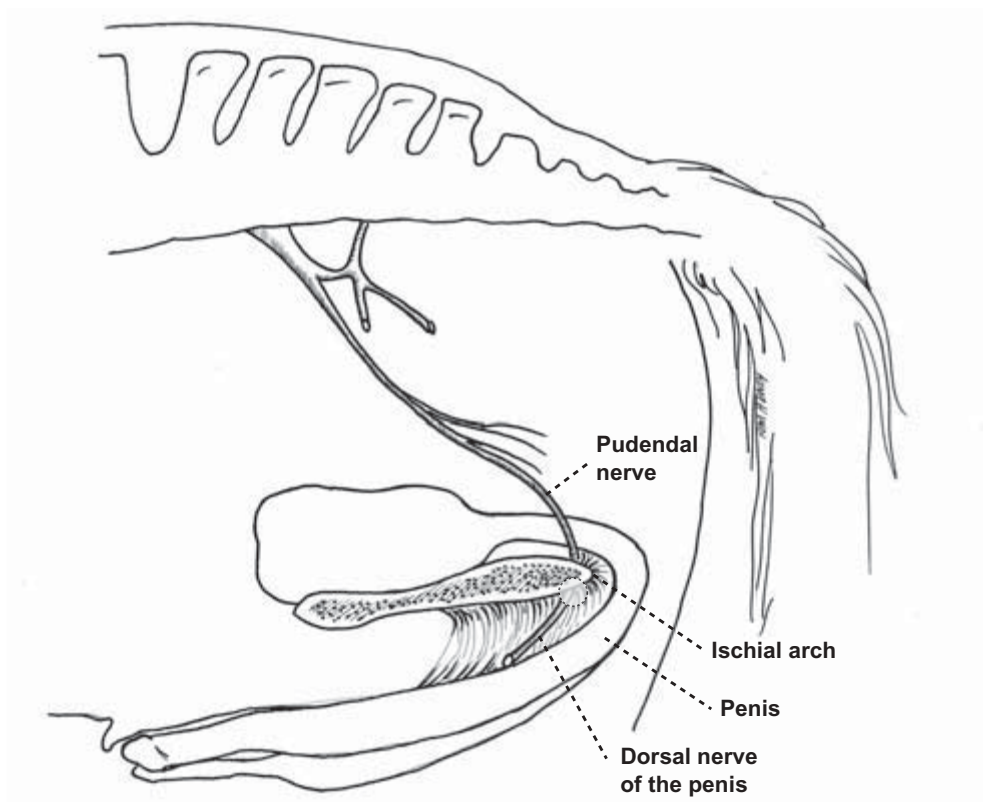
Fig. 18.2   Anatomical locations for pudendal nerve blocks of the penis.

B. Technique

- o   Insert a 21- or 22-gauge, 3.81 cm (1.5 inch) needle (angled ventrally toward the midline) at each site until the point of the needle contacts the ischial arch, where the pudendal nerves course around the ischium.
- o   Deposit 5 ml of local anesthetic adjacent to each nerve.
- o   The penis usually protrudes within 5 min.

C. Choice of anesthetic

- o   A short-acting local anesthetic, such as *lidocaine HCl*, should be used rather than *mepivacaine HCl* to avoid prolonged protrusion of the penis and prepuce, unless prolonged penile and preputial desensitization is required.

19   Anesthesia of the eye

Daniel S. Ward

Some form of sedation and local anesthesia is usually required for satisfactory ophthalmic examination of horses. In addition, these agents are often adequate for minor diagnostic and surgical procedures.

I. Restraint

- Intravenous sedation is invaluable for promoting cooperation for eye examinations and standing ocular surgical procedures in horses.
  - *Xylazine* (0.3 mg/kg, IV) for short-term (~ 10 min) sedation.
  - *Detomidine* (0.005 mg/kg, IV) for more prolonged sedation (~ 20 min).
  - *Butorphanol* (0.01 mg/kg, IV) may be added to either *xylazine* or *detomidine* sedation to reduce motion in fidgety horses.

II. Topical anesthesia

- Is generally used to facilitate examination of a painful eye.
- Allows the performance of minor diagnostic and surgical procedures of the cornea and conjunctiva.

A. Proparacaine and tetracaine

- Are the most commonly used topical anesthetics.
  - They are essentially interchangeable, although surface *toxicities* are more common with *tetracaine*.
- Onset of action in humans takes approximately 15 s, and the duration is approximately 15–30 min. These parameters are probably similar in horses.

B. Adverse effects of topical anesthetics

- Reduce *Schirmer tear* test values.
- Cause minor corneal epithelial damage (which can cause surface irregularities).
- Suppress wound healing with prolonged use.

Therefore, topical anesthetics should not be prescribed for pain relief.

III. Injectable local anesthesia

- Specific ocular nerve blocks are either *motor* or *sensory* blocks of the eye and adnexal structures.
  - ○ Sensory nerves are generally blocked more effectively than motor nerves.
- *Auriculopalpebral motor block* is the most important nerve block, but the sensory blocks listed may be helpful in certain minor surgical procedures of the eyelids.
- *Field blocks* and *infiltration anesthesia* are also important and are used primarily for sensory blockade.

A. Technique

- ○ Local anesthetic injections are accomplished using 25 gauge, 1 inch needles.
- ○ Injection volumes are usually 1–2 ml.
- ○ Injectable local anesthetics can be used for:
  - – Nerve block anesthesia.
  - – Field block anesthesia.
  - – Infiltration anesthesia.

B. Local anesthetic agents

- ○ Can be classified on the basis of duration of action:
  - – *Lidocaine*: short to medium duration (1–2 h).
  - – *Mepivacaine*: short to medium duration (1–2 h).
  - – *Bupivacaine*: long duration (4–6 h).

C. Adjunctive agents

- ○ May increase anesthetic effect and/or duration of action of local anesthetic.

Hyaluronidase
- ○ Mixed with local anesthetic (1500 IU/100 ml).
- ○ *Hyaluronidase* breaks down ground substance, allowing better diffusion of anesthetic.
- ○ Well documented effectiveness in retrobulbar anesthesia in humans, especially when combined with ocular compression.
- ○ Not evaluated in horses.
- ○ Only modestly helpful in retrobulbar blocks in cattle.

Epinephrine
- ○ Diluted (1:200 000) with *epinephrine* (0.1 ml of 1:1000) to 20 ml *lidocaine* (2%).
- ○ Resulting vasoconstriction increases anesthetic residence time in infiltrated area, as well as limiting systemic absorption of anesthetic.

Fig. 19.1   Sites for nerve block anesthesia of the eye and adnexa. The dashed line indicates the location of the orbital rim, and the dotted line indicates the location of the zygomatic arch; most blocks are placed along one of these two osseous structures. Sites of specific blocks are auriculopalpebral (1), which can be blocked at three different locations; supraorbital (2); lacrimal (3); infratrochlear (4); zygomaticofacial (5).
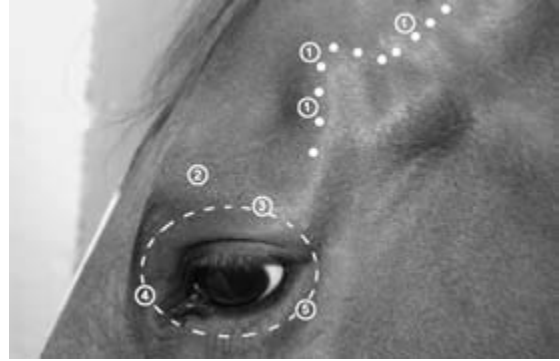
IV. Motor nerve blocks

- **Auriculopalpebral nerve** (see Fig. 19.1).
  - Terminal branch of the facial nerve (seventh cranial).
  - Courses over the zygomatic arch, giving off the rostral auricular branch to the auricular plexus and the zygomatic branch to the orbicularis oculi muscle.
  - Motor to the *orbicularis oculi muscle*.

  Auriculopalpebral nerve block
  - Usually the only block necessary for diagnostic evaluation of the equine eye.
  - Location:
    – Block is usually performed where the nerve is palpated along the dorsal edge of the zygomatic arch just anterior to its highest point.
    – Can also block where the zygomatic arch meets the superotemporal aspect of the orbital rim or more caudally near the base of the ear.
  - Auriculopalpebral blocks diminish the blink response so *artificial tear* ointment should be applied following examination.

V. Sensory nerve blocks

A. Supraorbital nerve (see Figs 19.1 and 19.2)

- Terminal branch of the ophthalmic nerve (fifth cranial).
- Sensory to most of the *superior lid*.
- Arises from the frontal nerve through the *supraorbital foramen* along with the supraorbital artery.

  Supraorbital nerve block
  - Facilitates minor surgical procedures of the nasal portion of the superior lid.
  - As the supraorbital nerve exits its foramen, its branches intermingle with terminal branches of the auriculopalpebral nerve.
    – Anesthetic deposited at the superficial aspect of the foramen will block some of these distal auricolopalpebral twigs and therefore have some effect on *motor* function of the orbicularis oculi muscle.
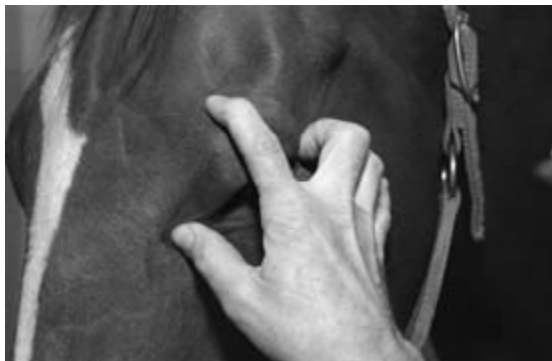
Fig. 19.2   Finding the location of the supraorbital foramen using Tóth's law. For the left eye, the thumb and middle finger of the right hand are placed at the nasal and temporal canthi, respectively. The index finger will then fall on, or near, the supraorbital foramen.

- – However, a well placed proximal auriculopalpebral block alone should be effective for motor blockade, and the supraorbital nerve, strictly speaking, is a *sensory* nerve.
  - o Location:
    - – The supraorbital foramen is palpable on the superior orbital rim just as the rim starts to widen nasal to its midpoint.
    - – Tóth's law states that if the thumb and middle finger of the right hand are placed at the nasal and temporal canthi (respectively) of the left eye, the index finger will fall on, or near, the supraorbital foramen (see Fig. 19.2) .
  - o Technique:
    - – Insert needle into the foramen and after aspirating (to ensure avoidance of supra-orbital artery), inject as needle is withdrawn.

B. Lacrimal nerve

- o A branch of the ophthalmic nerve, it runs along the dorsal rectus muscle to ramify in the lacrimal gland and upper eyelid.
- o Sensory to the *temporal canthus* and temporal *25% of the superior lid*.
- o Blocked along the superior orbital rim just nasal to the temporal canthus (see Fig. 19.1).

C. Infratrochlear nerve

- o Branch of the nasociliary nerve, which itself is a branch of the ophthalmic nerve.
- o Sensory to the nasal canthus.
- o Blocked at its location within a notch in the superior orbital rim near the nasal canthus (see Fig. 19.1).

D. Zygomaticofacial nerve

- o Terminal branch of the maxillary nerve.
  - – Also derives twigs from the zygomaticotemporal and lacrimal branches of the ophthalmic nerve.
- o Sensory to the temporal 75% of the *inferior lid*.
- o Blocked at the inferior orbital rim adjacent to the temporal canthus (see Fig. 19.1).

VI. Deep orbital nerve blocks

A. Nerves blocked

- Local blocks placed deep within the orbit provide anesthesia and akinesia of the globe by their actions on the *oculomotor*, *trochlear*, *trigeminal* (ophthalmic branch) and *abducens* nerves, all of which enter the orbit near the orbital apex.

Oculomotor nerve
- Motor to the dorsal, ventral and medial rectus muscles the inferior oblique muscle, the levator palpebra muscle, and the papillary sphincter muscle.

Trochlear nerve
- Motor to the superior oblique muscle.

Trigeminal nerve
- Sensory to the eye and ocular adnexae.

Abducens nerve
- Motor to the lateral rectus and retractor bulbi muscles

B. Techniques

Four-point block
- A 20-gauge 3 inch needle is inserted into the orbit at the 12:00, 3:00, 7:00 and 9:00 positions (*6:00 should be avoided to minimize the chance of damaging the optic nerve*).
- A slight 'pop' is felt as the orbital septum is penetrated; if the needle does not penetrate the septum, anesthetic may migrate subconjunctivally.
- Deposit 5–10 ml of anesthetic at each site.

Peterson-type block
- This is a modification of the Peterson deep orbital block used in cattle.
- A slightly curved 18-gauge 10 cm needle is inserted 1 cm temporal to the temporal canthus and directed inferonasally towards the opposite nasal canthus.

C. Potential complications of deep orbital blocks

- Retrobulbar hemorrhage, inadvertent penetration of the globe, and laceration of the optic nerve.
- Sudden death has been reported anecdotally following deep orbital blocks in cows, presumably due to injection of anesthetic into the subarachnoid space of the optic nerve which is contiguous with the subarachnoid space of the brain.

VII. Field block (line block) anesthesia of the eye

- Deposition of a line of local anesthetic along the superior and/or inferior orbital rims will effectively block all motor and sensory innervation to the eyelid(s), greatly facilitating surgical procedures and subpalpebral lavage apparatus placement.

VIII. Infiltration anesthesia of the eye

- Refers to injection of local anesthetic agent into tissue without regard for the course of nerves supplying the area of interest.
- Motor and sensory innervation of the infiltrated area will be affected, with the sensory component usually affected to a greater extent than the motor component.
- This technique generally requires larger volumes of anesthetic agent, and can affect tissue architecture or cause histopathology if applied overzealously.

20   Analgesia

Physiological basis of pain management

Alex Livingston

I. Introduction

A. Treatment of pain

- The appropriate treatment of pain in the horse is particularly dependent on two factors:
    - The ability to *recognize* and *diagnose* the presence of pain.
    - The appropriate *choice of analgesic* strategy.
- Recently, additional factors have become relevant in the treatment of pain:
    - The recognition of the value of *pre-emptive analgesia* to reduce sensitization to subsequent pain.
    - The development of the concept of *balanced analgesia*, using several analgesic drugs to address pain in a structured manner.

B. Strategies for analgesia

- Many of these strategies have arisen from an increased knowledge of the various mechanisms in the body that are associated with pain.
    - Whilst much of this new knowledge is based on human and laboratory animal studies, it would appear that the principles can be applied to all animals.
- What is apparent from these studies is that pain is a *complex* and *dynamic* entity and may show many variables both in nature and duration, and that we must consider many factors when deciding on a treatment protocol.
- *Dynamic factors* include changes in the pain intensity over time.
    - It should be recognized that pain may get better or worse with time.
    - It is appropriate to modify the dose or route of analgesics over time.
- Changes may also be seen in the *nature* of pain over time.
    - For example, the use of surgery to correct a chronically painful condition:
        - chronic, low-grade pain is perhaps replaced by acute, high-grade pain immediately after surgery.
        - This may then be replaced by intermittent neuropathic pain, associated with failure to prevent central sensitization, after surgery.
    - Obviously, a strategy involving more than one analgesic agent or preparation will best address the pain management in such a case.
    - Furthermore, the different pain modalities in such a situation may elicit different pain-related behavior, and it is only by the accurate recognition of these behaviors that appropriate dosing and choice of analgesic agents will be achieved.

C. Nociception

- ○ The difficulty with the concept of animal pain is that pain itself is a *perception*, and as such is something that exists only in an individual's higher cognitive center.
    - – Thus, if one person cannot accurately conceive what another person is perceiving as pain, how can we conceive what a horse is actually feeling?
- ○ The solution to this dilemma is to focus on the *processes* that take place and to recognize their significance in the perception of noxious stimuli.

D. Process of nociception

- ○ The process of nociception refers to the detection, transduction, and transmission of a noxious stimulus from the site of stimulation to the higher centers of the central nervous system.
- ○ In 1983 the International Association for the Study of Pain defined *pain* as, '*an unpleasant sensory experience associated with actual or potential tissue damage, or described in terms of such damage.*'
    - – This clearly refers to human perception of pain.
- ○ Various addenda have been made, but with regard to animals we are still bedevilled with the evaluation of pain as it relates to human experience.

II. Anatomy and physiology of normal nociception

- As far as we can tell, the general anatomic and physiologic mechanisms associated with nociception are remarkably similar in most mammalian species.
- The greatest differences occur in the *behavioral* responses to similar stimuli.

A. Anatomy

- ○ Although there are obvious skeletal, muscular, and visceral anatomical differences between horses and other mammals, the various tissues and organs are served by a very similar series of nerves and nervous inputs.
- ○ There are some aspects of equine anatomy that are reflected in particular nociceptive inputs, and these are reflected in specific behaviors associated with these inputs.

Examples
- ○ Equine hoof
    - – Represents a keratinized tip to an extended phalanx and as such is exposed to continuous wear. This wear requires continuous growth, which requires a highly vascular internal lamina construction.
    - – The importance of the hoof as a well innervated structure is associated with its function in balance and locomotion. Thus we have a highly vascular, highly innervated structure encased in a strong and rigid keratinized wall.
    - – Pathological changes in the laminated area resulting in inflammation and swelling can give rise to exceptionally painful inputs when they occur.

- o Equine large intestine
    - – The area of fermentation of the gut contents, being a blind-ended sac with a covering of well innervated peritoneum, is particularly sensitive to dilation compared with the open-ended, highly keratinized system in ruminants.
- o The horse also has highly developed *visual* and *olfactory* systems which are also well innervated and sensitive to damage.

B. Physiology

- o The specialized anatomical characteristics are not matched in the same way by the sensory/nociceptive systems.
- o It would appear that the *sensory* endings in the various tissues of the horse are similar to those in other mammals, representing pressure, heat, cold and combinations of these (*polymodal*).

Ascending pathways

- o The neurons transmitting nociceptive information to the CNS appear to be myelinated Aδ and unmyelinated C fibers.
- o These fibers seem to access the spinal cord via the dorsal root and interact with other systems, particularly in the dorsal horns of the spinal grey matter at the levels of laminae l and 2.
    - – These interactions allow transfer of information to various regions including the ventral horn (to facilitate spinal reflex responses), the contralateral regions of the spinal cord, as well as some ipsilateral areas (to allow ascending information to be processed and to interact with a complex series of regions in the hind- and mid-brain such as the ventromedial medulla), the nucleus raphe magnus, the locus coeruleus, and the periaqueductal gray.
- o These regions also interact with higher centers such as the lateral hypothalamus, the anterior pretectal area and the prefrontal cortex.
- o In addition, the nature of the responses to noxious stimuli in the horse indicates that the central interactions are just as complex as those of any other mammal.

Descending pathways

- o The complex descending pathways that return from the higher centers to modify the spinal inputs also appear to be similar to those of other mammals.
- o The descending inhibitory pathways associated with nociception are particularly important since they represent the sites of action of some of the most significant pain-modulating pharmacological agents.
- o Descending pathways originate in the *periaqueductal gray* and other relay areas previously mentioned and interact with the neurons in the dorsal laminae of the spinal gray matter to modify the incoming nociceptive stimuli. It is at this level that the 'gating' mechanisms that control input to the higher areas, and thus the level of *awareness* of pain, take place.

III. Neurotransmitters

- It would appear that most mammals have similar neurotransmitters involved in the various synaptic connections of the nociceptive neuronal systems.
- This is evidenced by the fact that most pharmaceutical agents that interact with the nociceptive systems to produce analgesia in humans have the same actions in animals.

A. Sodium channels

- ○ *Local analgesics* are the simplest group of agents to interfere with the nociceptive system.
    - – They generally act by blocking *sodium channels* in excitable tissues.
    - – Sensory receptors and sensory nerves, as well as motor nerves and different types of muscle, depend on sodium channels for their ability to depolarize and initiate impulses.
    - – We now know that there are several different kinds of sodium channels with different structures and physical characteristics, and future research may allow drugs with more specific actions and enhanced analgesic effects.
- ○ Rapid penetration of the local analgesic drugs is possible because the axons responsible for transmitting the nociceptive information are the smallest and the C fibers are unmyelinated.
- ○ The greatest advances have come in developing *techniques* to place analgesic drugs in particular sites (from the periphery to the spinal cord) to produce specific effects.

B. Endogenous opioids

- ○ Interact with receptors on a variety of neurons and mimic the actions of the endogenous opioid neurotransmitters, the peptide enkephalins and endorphins.
- ○ These agents are found in several areas of the CNS, particularly those associated with nociceptive processing such as the periaqueductal gray, the ventromedial medulla, and the dorsal horns of the spinal cord.
- ○ They inhibit neurons associated with the transmission of nociceptive information.
- ○ There are several endogenous opioid transmitters with actions on three main groups of receptors, known as mu, delta, and kappa receptors.
- ○ Different drugs show different affinities for the various receptors and show a range of side effects on systems (e.g. cardiovascular and respiratory) and different degrees of sedation. (See Chapter 11.)
- ○ The endogenous opioids in the spinal cord are part of the *descending inhibitory system* described earlier.
- ○ There is some evidence of species variation in the actions of these agents.

C. Catecholamines (alpha$_2$ adrenoceptor agents)

- ○ *Norepinephrine* (NE) is the catecholamine most directly involved in nociceptive processing.
- ○ Like the endogenous opioids, NE is closely involved with the *descending inhibitory system*, particularly at the level of the spinal cord although there are also sites of action at higher levels.

○ NE is thought to act at the α_2 receptor site as an inhibitory neurotransmitter reducing the central input of nociceptive neurons.

○ Specific α_2 adrenoceptor agents produce analgesia and sedation in horses, but these effects appear to be less profound than in ruminants.
  – This suggests a degree of species variation in the role of catecholamine neurotransmitters.

D. Amino acids

○ Amino acids are the most common neurotransmitters within the CNS.

○ Glutamate has *excitatory* effects on most neurons and acts via several different receptors.

○ Gamma amino butyric acid (GABA) is the most common *inhibitory* neurotransmitter in the CNS, again with actions on more than one receptor site.

○ The range of activities of these neurotransmitters makes them too non-specific to use on nociceptive systems.
  – However, drugs which mimic some of the actions of GABA are used as anesthetics, and agents which interact with glutamate receptors may play a role in treating or preventing certain pathological pain conditions.

E. Peptides

○ There are many other peptide agents within the nervous system besides the enkephalins and endorphins previously mentioned.

○ Perhaps the best known of these is *substance P*, a peptide found in the dorsal horn of the spinal cord.
  – It is intimately involved with the transmission of the nociceptive input from the dorsal root into the dorsal horn of the spinal cord and its upward transmission to the brain.
  – It has also been shown to have a role within the brain associated with pain pathways.

○ Other peptides, which have been suggested to have involvement with nociceptive processing include *neurotensin*, *somatostatin*, *neurokinin*, *galanin*, *calcitonin gene-related peptide* and many others.

○ Reliable modulation of these agents to produce analgesia has not been shown in domestic animals, although research into their modes of action and potential for manipulation continues.

F. Miscellaneous neurotransmitters

○ There are other similar neurotransmitters in the CNS such as dopamine and 5-hydroxytryptamine (5HT).
  – 5HT clearly has interactions with nociceptive processing within the CNS.
  – However, it also has the potential to interact with a very large number of different receptors and receptor subtypes and has actions on a wide range of neural functions, many associated with behavioral control.

○ Drugs which interact with 5HT are rarely used as analgesics due to the wide range of side effects.

IV. Pathology

- The normal, healthy nociceptive system in animals has the ability to effectively and rapidly transmit information about nervous stimuli in the periphery to the brain and to elicit the appropriate responses (as previously described).
- However, recent studies have shown that the responses of the nervous system to noxious stimuli are not static 'hard-wired' events.
  - The very existence of a noxious stimulus can change both the ability of the peripheral receptor to respond to a stimulus and the perception of that response at the level of the brain.
- We can distinguish the earlier described systems as *physiological* responses whilst the altered systems can be classed *pathological* responses.
  - Pathological responses can be divided into *peripheral* and *central* '*sensitization*', both of which result in an augmentation of the perception of the stimulus.

A. Peripheral sensitization

- This is the best-known and easiest form to demonstrate and address.
- Basically, the sensitization results from agents released from damaged tissues causing an increase in the sensitivity of the nerve endings that they come into contact with.
  - These agents are often many and varied; their make-up may depend upon the nature of the insult, the tissue affected, the intensity of the damage, and the species.
- Types of agents released include: *cytokines*, *kinins*, *arachidonic acid* derivatives (leukotrienes and prostaglandins), H^+ and K^+, *peptides* and other agents (e.g. histamine).
- The net result of the interaction of these agents with the sensory nerve endings is an *increased sensitivity* to incoming stimuli, which occurs in *two main ways*.
  - The first is the simple *lowering of the threshold* of the sensory endings.
    - The nerves start to transmit impulses at a lower level of input stimulus and produce more impulses for a given stimulus.
  - The second is that nerves that previously transmitted information that was not perceived as pain (e.g. warmth or touch) now transmit that information as pain.
  - These effects are also characterized by the development of larger areas of 'influence' around the lesion.
    - Thus a stimulus that would have been perceived as painful over a small area develops to record pain over a much larger area.
  - In human medicine, the two sensitizing effects are described as *hypersensitivity* and *allodynia* respectively.
  - It has been easy to demonstrate hypersensitivity in animals, but because of our inability to understand the perception of stimuli which do not normally produce an aversive response we can only surmise the existence of allodynia in animals.

B. Central sensitization

- The concept of *central sensitization* was developed some 20 years ago and has promoted the concept of *pre-emptive* analgesia.

- ○ Simply put, the concept suggests that when the CNS component of the nociceptive pathways is exposed to excessive and prolonged sensory input, the pathways become more sensitive to input stimuli and the thresholds that are perceived as painful become lower (i.e. the system becomes 'sensitized').
- ○ This process has been demonstrated in several species including man.
- ○ Although the concept was originally questioned, it is now generally accepted that if exposure to pain during surgical procedures that involve tissue and nerve damage is effectively blocked or reduced, then the perception of postoperative pain is reduced and the development of chronic neuropathic pain is attenuated.
  - – One hurdle that had to be overcome was to understand that general anesthetics *do not* block the *afferent nerve barrage*. Thus central pain sensitization could occur even with an adequate level of anesthesia, since the unconsciousness and amnesia of the anesthetic did not block, or reduce significantly, the activity of nociceptive neurons.
  - – Of course, this is obvious when one considers that experiments recording nerve activity had been made in anesthetized laboratory animals for decades.
- ○ Central sensitization is not easy to demonstrate, as a degree of peripheral sensitization may take place concurrently.
  - – One way to demonstrate the concept of central sensitization is to compare the postoperative analgesia needs in two groups of patients having the same surgery and anesthesia. One of the groups is given a local anesthetic regional block prior to surgery, while the control group is given a saline injection.
  - – Reliably, the group with the preoperative block requires less postoperative analgesia than the control group, although the preoperative block will have worn off by the postoperative time.

C. Central sensitization and the horse

- ○ The existence of central and peripheral sensitization in the horse has been demonstrated.
  - – Thresholds to pain were measured in the legs of horses that had received an experimental tendon injury, in terms of the effectiveness of a postoperative analgesic injection.
  - – The study showed that, not unexpectedly, the *injured limb* was much more sensitive to pain following the injury compared with before, even in the presence of an analgesic dose of *detomidine*.
  - – The *uninjured limb* showed a similar, though lesser, pattern of pain sensitivity.
  - – This suggests that what was seen in the uninjured limb was central sensitization, whilst the injured limb demonstrated a *combination* of central and peripheral sensitization.

D. Process of central sensitization

- ○ Research studies have shown that the process of central sensitization involves the neurotransmitter glutamate, probably acting through its NMDA receptor.
- ○ There are some drugs that act to block or antagonize this receptor such as *ketamine*, *amantidine*, and *gabapentin*, and these have been used to treat and reduce the chronic postoperative neuropathic pain states as well as to prevent its development.

V. Balanced analgesia

- *Balanced analgesia* is the term used to describe a situation in which more than one analgesic regimen is used in combination to achieve optimum pain control for a particular situation, with the lowest risk of side effects.
- The types of agent used in these various combinations could include local anesthetics, opioids, α_2 agonists, NSAIDs, corticosteroids, and NMDA antagonists.
  - *Example 1*. A surgical case involving laparotomy could include:
    - An α_2 agonist to provide presurgical sedation and analgesia.
    - An NMDA antagonist (e.g. *ketamine*) for induction.
    - An inhalational drug or TIVA for general anesthesia.
    - Intraoperative analgesics such as *ketamine*, *lidocaine*, or α_2 *agonists*, alone or in combination with inhalational anesthetics.
    - NSAIDs.
  - *Example 2*. A less complicated case involving suturing of the perineal region.
    - An α_2 agonist and opioid to produce sedation and analgesia.
    - Followed by an epidural with a local anesthetic and α_2 agonist.
    - A post-surgical NSAID for follow-up pain control.
- Another aspect of balanced analgesia is the *amount of drug* that should be given.
  - We should give enough drug, in the right way, to control the pain; otherwise there is no point in giving it.
  - Therefore, the correct dose is the one that works. For this to be efficacious, we have to be able to *recognize the signs of pain* associated with what the animal is experiencing, and adjust the dose or the drug regimen until the signs are relieved.
  - This also requires that we are able to recognize the signs of *overdose* of the drug(s) in use. If we reach this point without achieving pain control, then we must re-think our strategy or choice of drug or route of administration.
- Finally, we must also be aware of the *duration of action* of the different agents available, and be prepared to renew or review our choice after the appropriate time, until the horse is substantially pain free in the absence of medication.

Recognition of pain

Deborah V. Wilson

- Being a prey species, horses are very adept at hiding pain and discomfort, and this is part of the reason for the historical under-treatment of pain in this species.
- Horses also readily display a flight-or-fight response.
- Additionally, *quantification* of the pain experience is very difficult.
- In the absence of reliable *objective* measures of pain, the assessment of *behavioral changes* associated with pain provides some measure of the pain experience in the horse.

A. Normal behaviors

  - A normal stabled horse is very interested in its environment, alert and responsive to visitors, and eats for a large part of the time.

o   A horse not affected by visceral or musculoskeletal pain will continually move around the stall.

B. Behaviors associated with superficial pain

o   Horses will react forcefully to sources of superficial pain, either with vigorous avoidance or with aggression towards the source.

C. Behaviors associated with visceral pain

o   *Behavioral changes* associated with visceral pain include:
  –   Pawing, flank watching, rolling and sweating in cases of severe abdominal pain.
  –   Milder abdominal pain is associated with more subtle changes in behavior.
  –   Position of the head is consistently at or below the level of the withers.
  –   A number of additional signs can be observed in horses with visceral pain. (See Table 20.1.)

Pleural inflammation
o   Can be more painful than abdominal pain.
o   Pleuropneumonia is associated with reduced appetite and often severe weight loss, as well as the pain-associated behaviors described below.
o   Some of the behavioral changes displayed by a horse in pain are similar regardless of the source of the pain.

D. Behaviors associated with musculoskeletal pain

o   Musculoskeletal pain is *more obvious* than visceral pain; horses cannot hide musculoskeletal pain as readily as they can hide pain from other sources, particularly when they ambulate.
  –   It is easy to identify a horse that has the severe pain associated with the foot or joint since this pain affects weight-bearing.

Table 20.1   Signs associated with visceral pain in the horse.

Observed feature	Normal	Mild pain	Moderate pain	Severe pain
Ear position	Forward	Changes	Half mast	Back, little movement
Focus of attention	At door	At door	At wall, changes if approached	At wall, no change if approached
Eyes	Bright, alert	Bright	Dull, responds	Dull, no response
Mentation	Alert, orients	Alert, orients	'Sleepy', but responds	'Sleepy', no response
Stress	None apparent	None apparent	Mild distress Tachypnea Tachycardia	Sweating Distressed Tachypnea Tachycardia

Reprinted with permission from Sellon, D.C., Roberts, M.C., Blikslager, A.T. and Ulibarri, C.T. (2002) *AAEP Proceedings* **48**: 244–246.

     ○ The features that allow grading of lameness assist in grading the severity of musculoskeletal pain.

       – Back pain is much harder to quantify.

     ○ Behaviors demonstrated in horses with severe musculoskeletal pain include:

       – Dull expression.

       – Head at or below the level of the withers.

       – Little or no interest in visitors or food.

       – Little interest in activities outside stall.

       – Sweating and tachypnea may be evident.

       – Increased weight shifting, a gait change, or lack of weight-bearing may be evident.

       – In some cases the horse will become recumbent.

E. Chronic versus acute pain behaviors

     ○ Chronic pain produces more *subtle* changes in behavior and is harder to detect.

     ○ Chronic pain of musculoskeletal origin is usually associated with *atrophy* of the muscles of the affected limb, and overall weight loss.

     ○ Chronic laminitis is predominantly associated with gait changes and abnormal hoof growth.

Analgesia for acute pain

- Traditionally, analgesia has received limited attention in the horse, but it is extremely important for humanitarian and pragmatic reasons.
- Adequate pain management should improve the clinical outcome.
- Pain management is important in certain medical conditions (e.g. laminitis), post-surgery, and in the trauma patient.

I. Non-steroidal anti-inflammatory drugs (NSAIDs)

- Useful to treat mild to moderate inflammatory pain.
- Can be combined with more potent analgesics (e.g. opioids).
- Can be administered orally for chronic pain (e.g. osteoarthritis).

A. Flunixin meglumine (0.25–1 mg/kg, IV, IM; q8h)

     ○ Used for acute abdominal pain.

     ○ Used for postoperative analgesia.

B. Phenylbutazone (2–4 mg/kg, IV, PO; q12h)

     ○ Irritant to tissues.

       – Must *not* be given IM.

     ○ Used for postoperative orthopedic pain.

    o Used for chronic orthopedic pain.
      – Primarily in oral dosage form.
    o Mules and donkeys may require more frequent administration than horses.

  C. Ketoprofen (2 mg/kg, IV; q24h)

    o Has a central analgesic action in addition to anti-inflammatory effect.

  D. Carprofen (0.7 mg/kg, IV; q24h)

    o More slowly metabolized in donkeys.

II. Opioids

  • Useful for moderate to severe pain.
  • Risk of behavioral excitatory effects.
    o More likely with IV injection.
    o Less likely to occur in the painful horse.
  • Ileus is a risk, especially with repeated administration.

  A. Morphine (0.1–0.3 mg/kg, IM; q4–6h)

    o Ileus may be more likely than with other opioids (e.g. *butorphanol*).

  B. Butorphanol (0.02–0.04 mg/kg, IM, IV; q2–4h)

    o CRI following bolus (0.02 mg/kg); CRI: 0.024 mg/kg/h.

  C. Methadone (0.1 mg/kg, IM, IV; q4–6h)

  D. Meperidine (1–2 mg/kg, IM; q2–4h)

    o IV administration may cause hypotension (histamine release).

III. Tramadol

  • Useful for moderate to severe pain.
  • Dose: 1–2 mg/kg, IM, IV; q4–6h.
  • Not extensively studied in the horse.

IV. Alpha$_2$ agonists

  • Useful for moderate to severe pain.
  • Risk of ileus with repeated administration.

- Sedation accompanies analgesia.
- Mostly used for control of acute intense pain (e.g. colic).
- CRIs of α_2 agonists can be used for short-term control of acute pain.

Dosage range:
   Detomidine: (0.005–0.02 mg/kg; IV).
   Xylazine: (0.3–1 mg/kg; IV).
   Medetomidine: (0.0035–0.007 mg/kg; IV).
   Romifidine: (0.03–0.1 mg/kg; IV).

V. Ketamine

- Subanesthetic doses are analgesic.
- IM dose: 0.2 mg/kg (30–60 minutes of analgesia).
- IV dose: 0.2 mg/kg, IV, with sedation (e.g. *xylazine* 0.3 mg/kg, IV).
  - Use when α_2 alone is ineffective in controlling acute, intense pain.
- CRI bolus: 1 mg/kg, IV, over 30 min; CRI: 0.4–1.0 mg/kg/h.
  - Has not been evaluated for its analgesic efficacy.
  - No adverse effects noted in this dose range.
- Can be combined with *lidocaine* for infusion (see *lidocaine* below).

VI. Lidocaine

- Useful for treating mild to moderate pain.
- Bolus: 1.5–2.0 mg/kg, IV, over 5–10 min; followed by a CRI (3 mg/kg/h).
- In combination with *ketamine*.
  - Same dose of *lidocaine* + *ketamine* (bolus: 1 mg/kg IV, over 30 min; CRI: 0.2 mg/kg/h).

VII. Epidural analgesia (see Chapter 17)

VIII. Local nerve blocks of the limbs and head (see Chapters 16 and 18)

- Local nerve blocks of the limbs and head can be used to provide analgesia.
- Nerve blocks of the distal limbs are especially suited to this purpose.
  - It is especially important that the absence of limb fractures is verified before using nerve blocks for acute analgesic purposes.

21 Complications and emergencies

Anaphylactic and anaphylactoid reactions

I. Anaphylaxis

- An uncommon, but serious, complication of anesthesia.
- Defined as an exaggerated response to a foreign substance (antigen) to which there has been previous exposure and sensitization.
- Is an antigen–antibody type I immediate hypersensitivity reaction.
  - A drug that is recognized as a foreign substance stimulates the production of IgE antibodies, which subsequently fix to mast cells and basophils.
  - Re-exposure to the drug results in antibody binding to the antigen and release of a variety of chemical mediators (e.g. histamine, leukotrienes, bradykinin, and platelet activating factor) that may have profound physiological manifestations resulting in clinical signs of anaphylaxis (e.g. bronchospasm, shock).
- Unfortunately, immunologic reactions are generally *not* dose-dependent; therefore, test dosing is not clinically safe.

II. Anaphylactoid reaction

- Clinically is the same as an anaphylactic reaction.
- Involves a non-immune mechanism that causes direct stimulation of histamine release (e.g. *meperidine* when administered IV).
- Previous sensitization is not required.

III. Incidence and causative drugs

- Incidence of anaphylaxis during anesthesia in people is estimated at between 1 in 10 000 and 1 in 20 000.
  - Data are not available for horses.
- Mortality rate is < 5%.
- Causative drugs implicated in *people* include:
  - Neuromuscular blocking drugs in over 60% of cases.
    - *Rocuronium* and *atracurium* are most commonly implicated.
      - *Rocuronium* causes an anaphylactic reaction.
      - *Atracurium* causes an anaphylactoid reaction.
  - ~ 15% due to latex.

- ○   ~15% due to antibiotics.
- ○   4% are caused by colloid solutions.
- ○   Other drugs implicated include opioids and amide local anesthetics.
- ○   Inhalational anesthetics have not been implicated.
- Reports of reactions in *horses* have included antibiotics (penicillins) and contrast media (*diatrizoate*).

IV. Clinical manifestations

- Clinical signs range from mild non life-threatening anaphylaxis to severe anaphylactic shock and death.
- Signs may progress slowly or rapidly and appear at any time during anesthesia, although they are more likely to occur shortly after drug administration.
- Signs are related to the pathophysiological effects that result from the action of the released chemical mediators.
  - ○   These effects include profound vasodilation and increased vascular permeability.
- The reduction in circulating blood volume that results from transudation of fluid (i.e. edema) is estimated to be as much as 37%.
- Anaphylactic reaction is initially recognized by desaturation, difficulty in lung inflation, decrease in ETCO$_2$, and weak pulse.
  - ○   Signs include cardiovascular collapse, arterial hypotension, cardiac arrest, broncho-spasm, airway obstruction, pulmonary edema, cutaneous signs.
    - –   Cardiovascular collapse and bronchospasm are more frequent with anaphylaxis.
    - –   Cutaneous signs (e.g. wheals) are more frequent in anaphylactoid reactions.

V. Treatment

- Discontinue administration of inciting substance, if applicable.
- Provide oxygen
- Initiate positive pressure ventilation.
  - ○   In the anesthetized horse, discontinue anesthetic administration and ventilate with oxygen.
- Monitor the cardiovascular system.
  - ○   ECG.
  - ○   Blood pressure.
- Cardiovascular support.
  - ○   Fluid therapy and volume expansion.
  - ○   Catecholamines:
    - –   *Epinephrine*'s alpha and beta agonistic effects for counteracting the cardiovascular changes.
    - –   Use of pure alpha agonists has been recommended in people refractory to *epinephrine*'s actions on restoring effective spontaneous circulation.
    - –   The alpha agonistic effects restore the diastolic blood pressure, counteracting myocardial hypoperfusion, ischemia, cardiac failure, and malignant arrhythmias.
  - ○   *Atropine* to increase heart rate, if necessary.

- Bronchodilators.
  - β_2 agonists (e.g. *albuterol*) to treat bronchospasm.
  - *Atropine*.
- Corticosteroids.
  - For late-phase reactions.
- Antihistamines
  - Histamine antagonists (H_1 and H_2) for urticaria and pruritus.

VI. Identification of an allergic reaction

- Identification of the cause is difficult, and investigation of an allergic reaction should include a detailed history.
- Increased histamine concentrations following the adverse reaction will confirm the diagnosis.
- Increased serum *tryptase* concentrations (>25 µg/liter) will confirm an anaphylactic mechanism; however, a negative test does not rule out anaphylaxis.
  - Tryptase is a protein contained within mast cells that reaches peak plasma concentrations within 1 h after degranulation of the cell; therefore, serum samples should be taken shortly after the reaction.
- Intradermal skin- or prick-tests can be performed 6 weeks after the reaction.

Intraoperative hypotension

- Hypotension is a common occurrence in the horse, especially when inhalational anesthetics are used for maintenance of anesthesia.
- The incidence of hypotension is greatly reduced, as is the degree of hypotension, when anesthesia is maintained with injectable anesthetics (TIVA) or a combination of injectable and inhalational anesthetics (PIVA).
- In *adult* horses, there is a strong correlation between intraoperative hypotension and postoperative myopathy.
  - Maintaining the mean arterial pressure >70 mmHg reduces the incidence of myopathy.
- *Neonatal foals* have lower blood pressure than do adults due to the lower vascular tone of foals.
  - A mean arterial pressure of 40−60 mmHg is generally acceptable in the neonate.

I. Causes of hypotension

> Blood pressure = Cardiac output (Stroke volume × Heart rate) × Vascular resistance.

A. Myocardial depression

- All inhalational anesthetics cause myocardial depression.
  - Myocardial depression is most profound with *halothane*.

○ Stroke volume decreases due to decreased cardiac contractility.
○ Endotoxemia (e.g. gastrointestinal emergencies, neonatal bacteremia) contributes to cardiac depression.
   – Cardiac depression may result from a direct effect on the myocardium and/or result from a decrease in ionized calcium secondary to the endotoxemia.

B. Changes in vascular resistance

○ A decrease in vascular resistance leads to a decrease in blood pressure.

C. Bradycardia

○ Occasionally, bradycardia will result in a decrease in cardiac output and arterial pressure.
○ Bradycardia is usually transient and only rarely needs to be treated.

D. Hypovolemia

○ Decreased intravascular volume results in decreased preload and stroke volume.

II. Treatment of hypotension

A. Inotropes

○ Many hypotensive states respond rapidly to an inotrope (e.g. *dobutamine*) indicating that myocardial depression is the cause of hypotension.
○ *Dobutamine* infused to effect (~ 0.5–5 μg/kg/min) is the inotrope of choice.
○ Calcium can be infused simultaneously (10–20 mg/kg) over the course of the surgery if the measured ionized calcium is low or likely to be low (e.g. intestinal emergencies).

B. Correct volume deficits

○ Ideally, existing volume deficits are corrected before anesthesia but this is not always possible.
○ A balanced electrolyte solution may be used alone, or combined with a colloid.

C. Check anesthetic depth

○ Confirm that the plane of anesthesia is not excessively deep.

D. Change anesthetic regimen

○ Reducing the end-tidal concentration of inhalational anesthetic and administering an injectable agent such as *ketamine* should reduce cardiovascular depression and improve blood pressure. (See PIVA.)

Intraoperative hypertension

I. Characterization

- Pre-existing hypertension such as primary (i.e. idiopathic or 'essential') hypertension or secondary (e.g. renal, endocrine, or pregnancy-induced) hypertension are conditions which are rarely, if ever, diagnosed in horses.
  - Therefore it is unlikely that a horse will be presented for surgery with an existing diagnosis of hypertension.
- In human patients, a diagnosis of hypertension is based on a systolic pressure > 160 mmHg and/or a diastolic pressure >95 mmHg.

II. Causes of hypertension

A. Inadequate plane of anesthesia

- The most common cause of hypertension.
- A sudden increase in arterial pressure may occur with surgical stimulation.
- Check that the horse has not become disconnected from the machine or from an anesthetic drug infusion.
- Signs indicating a light anesthetic plane may accompany hypertension.
  - *Purposeful* movement.
  - Ocular signs (active palpebral reflex, nystagmus).
- Heart rate increase usually does *not* accompany hypertension in this case.
- Hypertension should resolve upon deepening the anesthetic plane.

B. Drug-induced hypertension

Alpha$_2$ agonists
- Injection of an alpha$_2$ agonist causes a temporary increase in arterial pressure.
- This increase in pressure is usually short-lived, and a slight decrease in heart rate may occur concurrently.

Sympathomimetic drugs
- Hypertension may result from overzealous administration of sympathomimetic (e.g. *dobutamine*) drugs for cardiovascular support.
- The magnitude of hypertension can be dramatic if a β_1 agonist (e.g. *dobutamine*) is administered following a parasympatholytic drug (e.g. *atropine*).
  - Tachycardia will accompany hypertension in these cases.
- *Phenylephrine*, which is sometimes used intraoperatively in nephrosplenic entrapment, will cause hypertension due to vasoconstriction.

C. Miscellaneous causes

- Severe *hypercapnia*.
  - May be accompanied by excessive oozing from surgical site.

     o   Severe *hypoxemia*.
        –   The horse may be tachypneic, trying to 'buck' the ventilator, or gasping.
     o   *Hyperthermia* (see HYPP and malignant hyperthermia).
     o   *Tourniquet placement* has been identified as a cause of hypertension in anesthetized horses.
        –   Tachycardia is present concurrently.
        –   Hypertension develops soon after tourniquet placement and may increase in magnitude over time.
        –   Hypertension resolves when the tourniquet is removed.

Hypoxemia and hypoxia

Hanna-Maaria Palos

I. Definitions

A. Hypoxemia

     o   *Hypoxemia* refers to subnormal oxygen partial pressure in arterial blood.
     o   An arterial partial pressure of oxygen (PaO_2) < 60 mmHg (8 kPa) at sea level is considered the cutoff point for hypoxemia.
     o   However, this rigid definition may be misleading in some cases.
        –   For instance, a PaO_2 of 50 mmHg may be normal, for a 12-hour-old foal in lateral recumbency.
        –   A PaO_2 > 60 mmHg can also be subnormal (e.g. if the horse is breathing a higher fraction of oxygen).
     o   Hypoxemia has also been defined as a resting PaO_2 which is > 2 standard deviations below the normal PaO_2 for that animal's age at the particular inspired O_2 fraction.

B. Hypoxia

     o   Is a state of inadequate *tissue* oxygenation.
     o   Regardless of cause, insufficient O_2 eventually results in the cessation of aerobic metabolism and oxidative phosphorylation leading to *cell death*.
     o   The presence of hypoxemia does *not* necessarily imply that tissues are hypoxic.
        –   Oxygen delivery (DO_2) to the tissues must be considered when determining whether tissues are likely to be hypoxic.
        – DO_2 (ml/min) $= CaO_2 \times CO$

$$DO_2 = \left(1.36 \times Hb \times \frac{Hb\ \%Sat}{100} \right) + (0.003 \times PaO_2) \times CO$$

1.36 = ml of O_2 carried by 1 g Hb
CaO_2 = Arterial O_2 content
CO = Cardiac output (liters/min)
Hb = Hemoglobin (mg/dl)

Clinical signs of hypoxia
- o May be difficult to appreciate in an anesthetized horse.
- o Cyanosis may be present.
- o Tachycardia and hypertension due to hypoxia-induced catecholamine release.
- o The horse may be tachypneic, 'bucking' the ventilator, or gasping.

II. Causes of hypoxemia

A. Decreased inspired oxygen fraction (FIO_2)

- o *Comments*:
  - – An in-line oxygen analyzer will help to decrease the likelihood of this problem occurring.
  - – O_2 *flow* should be adequate to match O_2 *consumption* ($\sim$ 2.5 ml/kg/min in adult) and allow for loss due to leaks and O_2 aspirated from the system by gas analyzers.
- o Due to anesthetic machine failure in oxygen supply.
  - – Check that Y-piece is tightly attached to endotracheal tube.
  - – Turn off N_2O if in use.
  - – Check O_2 supply and pressures.
  - – Check that machine is properly connected to O_2 supply.
  - – Press O_2 flush to see if rebreathing bag fills.
    - ■ If rebreathing bag does *not* fill, check visible (accessible) O_2 hoses on the anesthetic machine.
    - ■ If a disconnected O_2 hose is not readily visible, the leak may be inside the machine.
  - – Small leaks in the system will be more likely to noticeably affect the FIO_2 if the fresh gas flow is low.
    - ■ A small leak in the machine (e.g. around soda lime canister) will contribute to a lower than expected $[O_2]$ but the mixture may not be hypoxic.
  - – If *compressed air* is being used to drive a ventilator bellows, a decrease in FIO_2 can result if a leak develops in the bellows.
    - ■ Contamination of the O_2 source, although unlikely, is possible.

B. Endotracheal tube

- o Check that the tube is properly placed.
- o Check that the cuff is adequately inflated.

C. Hypoventilation

- o Hypoventilation contributes to hypoxemia by virtue of the fact that an increase in alveolar partial pressure of CO_2 ($PACO_2$) reduces the PAO_2, and thus the PaO_2, according to the alveolar gas equation.

D. Ventilation perfusion (V/Q) mismatch

- o Lung regions with a low V/Q have a relative increase in perfusion.
  - – Supplemental O_2 will usually increase PaO_2 in situations of low V/Q ratio.

E. Shunt

- ○ In a pure shunt, there are areas of the lung with *no* ventilation.
  - – Supplemental O_2 will *not* be of benefit in pure shunt situations.

F. Decreased mixed venous O_2

- ○ Factors decreasing mixed venous O_2 (e.g. ↓ cardiac output, ↑ O_2 consumption) exacerbate the effects of V/Q mismatch and shunt on hypoxemia.

G. Pathological states likely to exacerbate hypoxemia

- ○ Distension of abdominal contents.
- ○ Pre-existing respiratory pathology (e.g. recurrent airway obstruction).
- ○ Acute pathological changes in the lung (e.g. inflammatory, pulmonary edema).

III. Causes of hypoxia

A. Decreased perfusion

- ○ Decreased cardiac output.
- ○ Vascular occlusion.

B. Hypoxemia leading to a decreased Hb saturation

C. Decreased oxygen carrying capacity

- ○ Anemia.
- ○ Toxicity (e.g. carbon monoxide poisoning).
- ○ Hemoglobinopathy (rare in horses).

D. Problems with O_2 transport from microvasculature to the cells

- ○ Vascular injury.
- ○ Edema.

E. Problems with oxygen utilization by the cell

- ○ Cyanide toxicity.

IV. Improving arterial oxygen content

A. Correct mechanical failures

- ○ Check anesthetic machine and ventilator.

B. Intermittent positive pressure ventilation (IPPV)

- ○ Instituting ventilation from the beginning of anesthesia is more effective in maintaining arterial oxygenation than trying to recruit collapsed alveoli.
  - – However, the resulting increase in intrathoracic pressure decreases venous return and, hence, cardiac output.
- ○ Optimize tidal volume (10–15 ml/kg).
- ○ Respiratory rate ranges are 6–8 breaths/min for adults and 8–12 breaths/min for foals.
- ○ If the horse is bucking the ventilator, check that the depth of anesthesia is adequate.
  - – Neuromuscular blockade is rarely indicated to correct this problem.

C. Optimize inspiratory: expiratory ratio

- ○ An increase in inspiratory time may optimize alveolar ventilation.
- ○ This may be especially important in cases of recurrent airway obstruction.

D. Optimize FIO_2

- ○ Increasing FIO_2 should increase PaO_2.
  - – This will not be true in the presence of a shunt.

E. Positive end-expiratory pressure (PEEP)

- ○ In some cases, application of PEEP (5–10 cmH_2O) may decrease atelectasis.
- ○ However, the increase in alveolar pressure may interfere with capillary circulation.
- ○ When PEEP approaches central venous pressure, venous return is reduced.

F. Aerosolized albuterol

- ○ *Albuterol* (beta$_2$ agonist) is reported to be beneficial in the treatment of hypoxemia in the anesthetized horse.
- ○ A dose of 2 μg/kg into the airways is recommended.
  - – Published method describes the use of a metered dose inhaler (MDI) canister (Ventolin, GlaxoSmithKline, Research Triangle Park, NC, USA), an MDI adapter (PriMed Co, Largo, FL, USA), and a PVC fitting.
  - – In the absence of specific equipment, *albuterol* (diluted to 10 ml in saline) can be administered into the endotracheal tube between respiratory cycles.
    - ■ This may be a less than ideal delivery method and may require higher or repeated doses.
- ○ *Albuterol* treatment prior to anesthesia may benefit horses with recurrent airway obstruction.

G. Improve cardiac output

- ○ Fluids and inotropes should be administered as indicated.

V. Postoperative hypoxemia

A. Causes

- ○ Hypoventilation following the cessation of IPPV, a decrease in FIO_2, and an increase in O_2 demand may all contribute to hypoxemia during the recovery period.
- ○ Other factors contributing to postoperative hypoxemia include:
    - – A decrease in the functional residual capacity (FRC) of the lung occurs in the anesthetized horse; this results in atelectasis and shunting which persist into the recovery period.
    - – Accumulation of secretions in the small airway compounds the effects of a decrease in FRC on atelectasis.
    - – Increased O_2 consumption during recovery, or as a result of shivering, will decrease mixed venous O_2 thus exacerbating the effects of shunting and V/Q mismatch.
    - – Inhalational anesthetics inhibit *hypoxic pulmonary vasoconstriction* which may contribute to shunting and V/Q mismatch.
    - – Decreased airway patency will contribute to hypoxemia.
        - ■ A patent airway must be established upon extubation.
        - ■ Nasal or nasotracheal tube placement, or intranasal *phenylephrine* administration will improve airway patency (see Chapter 3 – Airway management).

B. Supplemental oxygen

- ○ Increasing FIO_2, especially if O_2 is delivered intratracheally (10–15 liters/min) may increase PaO_2.

Hypercapnia

- ● Defined as a $PaCO_2$ above normal.
    - ○ $PaCO_2 > 45$ mmHg.
- ● Common during general anesthesia due to the depressant effects of anesthetic drugs on the respiratory center.
- ● Generally results from hypoventilation.
    - ○ On rare occasions, hypercapnia results from increased production of CO_2 as in malignant hyperthermia and hyperkalemic periodic paralysis (HYPP).

A. Effects of hypercapnia

- ○ Increased cardiac output due to sympathetic stimulation with mild hypercapnia.
- ○ Increased likelihood of hypoxemia due to a decrease in the alveolar oxygen partial pressure (PAO_2), particularly if the FIO_2 is low.
    - – For this reason it is advisable to provide supplemental O_2 for all but the shortest anesthetic procedures.
- ○ Increased cardiac irritability and decreased contractility.
- ○ Decrease in pH.
    - – The pH decreases by ~ 0.1 pH unit for every 20 mmHg acute increase in $PaCO_2$.
    - – So a $PaCO_2$ of 70 mmHg would decrease the pH by ~ 0.15 units.

Comment: One area of controversy in equine anesthesia practice is what constitutes acceptable hypercapnia! Many equine anesthetists tolerate a $PaCO_2$ up to 70 mmHg. Changes of this magnitude, although apparently well tolerated by the anesthetized horse, cause a significant decrease in pH.

B. Treatment of hypoventilation

- o Institute controlled ventilation.
- o If the horse is already being ventilated check:
  - – That the *tidal volume* is adequate (10–15 ml/kg in an adult).
  - – That the *ventilation rate* is adequate (6–8/min in an adult).
  - – Check that the *bellows* is intact and filling adequately to deliver an adequate tidal volume.
    - ■ Improper filling of the bellows may be a result of leaks in the system.

Intra-arterial and perivascular injections

- ● Intra-arterial injections usually involve the *carotid artery* and occur during failed attempts to insert a hypodermic needle or catheter into a jugular vein.
- ● The jugular vein is generally palpable and visible following its occlusion (achieved by placing a thumb in the jugular furrow).
  - o It may not be visible in thick-necked horses with a dense hair coat.
    - – In these cases, the jugular vein may have to be located by digital palpation.
  - o Clipping the hair will aid in locating the jugular vein.

I. Factors contributing to intracarotid injection

- ● Inadequate control of horse such that movement is occurring during injection or catheter placement.
- ● Poorly muscled horses and young foals in which the carotid is relatively superficial.
  - o Special care must be taken with jugular injections in these cases.
- ● Use of an unnecessarily long needle.
- ● Directing the needle too deeply and 'stabbing around' to locate the jugular vein.
- ● Injections in the lower neck or high up on the neck may be more likely to strike the carotid.

II. Verification of jugular puncture

- ● The colour of the blood may *not* be helpful.
  - o Venous blood can resemble arterial once it contacts the air.
- ● Use of a long, narrow-bore needle or catheter may *not* give an indication of being in the carotid.
  - o Flow of blood through the needle or catheter depends on the *bore* and *length*.
- ● If a suitably sized needle or catheter is placed 'pointing downwards' in the jugular vein, blood will not flow from the tip unless the vein is being occluded (assuming that the horse's head is up); this is *not* the case with carotid placement.

- When the venous occlusion is removed, blood should flow back down the needle or catheter; this is *not* the case with carotid placement.
  - It is important that *air* not be allowed to enter the circulation during this maneuver.

III. Sequelae of failed jugular injection

A. Hematoma formation

- Can develop rapidly after carotid puncture and distort the anatomy of the local tissues, making ipsilateral jugular venepuncture difficult or impossible.
- If carotid puncture is suspected, the area should be compressed with the flat of one hand while the other hand applies pressure to the contralateral side of the neck; maintain pressure for at least 10 min.

B. Recurrent laryngeal nerve damage

- Needle damage to the adjacent recurrent laryngeal nerve can result in *airway closure* on the affected side.

C. Horner's syndrome

- Defined as ptosis, miosis, and enophthalmos.
- May result from damage to the underlying sympathetic nerve trunk.

D. Esophageal injury

- Possible, although unlikely.

E. Tissue slough or abscess

- Either is possible following injection of an irritant substance.
- If inadvertent drug disposition occurs it is very important that every attempt be made to *flush* the area immediately with copious volumes of warm isotonic saline.

IV. Signs and sequelae of intracarotid injection

- Serious consequences result from intracarotid injections.
- Severity depends on the *substance* injected and the *volume* and *speed* of injection.
  - It is important to realize that transient central signs may even result from intracarotid injection of saline solutions.

A. Responses to intracarotid injection

- The CNS effects of arterial injection result from:
  - High concentrations of drug entering the brain.
  - The spasm of the carotid artery which results in cerebral hypoxia.

- *Immediate response* (e.g. excitement, staggering) indicates that the injection can't have been into the jugular vein.
    - Stop any further injection.
    - *This shows the importance of initially injecting slowly.*
- Responses vary from mild agitation to excitement and seizures.
    - In most cases, the horse crashes to the ground with legs thrashing.
    - If the horse flips over backwards landing on its poll, the outcome will most likely be fatal.
    - There is a great risk of injury to handlers, especially in a confined space.
    - Once recumbent, the horse may continue to thrash around for a few minutes.
    - Trauma to the head and eyes may result.

B. Treatment

- Aimed at controlling seizure activity.
    - *Diazepam/midazolam*, *thiopental*, *propofol* or combinations of these drugs given to effect.
- Provide oxygen.

C. Prognosis

- If the horse begins to calm down soon after the event and develops a normal breathing pattern, the prognosis is hopeful.
- The outcome is *fatal* in some cases.

Cardiopulmonary resuscitation

- Cardiac arrest in the anesthetized horse is responsible for ~ 30% of mortalities.
- Predisposing factors include:
    - An excessively deep anesthetic plane leading to cardiovascular collapse.
    - Hypotension.
- Prognosis for a successful outcome is poor due to the difficulty of performing cardiac resuscitation.
- While the success rate with CPR would be expected to be higher in foals, many neonatal foals undergoing anesthesia are physiologically compromised due to systemic illness thereby reducing the likelihood of success.

I. Treatment

- Follows general guidelines used in other species.
- Success is more likely if the horse is already intubated and receiving O_2.
    - Chances of success under field conditions, without an endotracheal tube and a means of ventilation, are minimal.
- Once cardiac arrest is detected, discontinue anesthetic administration.

A. **Airway**

o   Insert or secure endotracheal tube.

B. **Breathing**

o   Supply oxygen.
  –   Use a demand valve or mechanical ventilation.
  –   Ventilation rate: 6–10 breaths/min (use the higher rate for foals).

C. **Circulation**

o   Lack of peripheral pulse is an indication to initiate chest compressions.
o   Compression rate: 40–80 compressions/min.
o   Compression is achieved by having the resuscitator (a large person preferably) deliver a blow with the knee(s) immediately behind the horse's elbow area.
  –   Maximum force is achieved by delivering the blow from a standing position.
  –   The higher the compression rate the greater the blood flow.
  –   Even the best attempts are unlikely to achieve > 50% of baseline flow.

D. **Drugs**

o   *Epinephrine* (0.02 mg/kg, IV) to cause vasoconstriction and improve contractility.
  –   Alternatively, *methoxamine* or *phenylephrine* (0.02–0.06 mg/kg, IV) vasoconstrict without the dysrhythmic effects associated with *epinephrine*.
o   Once spontaneous circulation returns, it is recommended that drugs with specific cardiac (i.e. rate, contractility, rhythm) and vasoactive effects should be used to stabilize cardiac output and blood pressure.
  –   *Dobutamine* (~0.5–5 μg/kg/min, IV) for inotropic effects.
  –   *Atropine* (0.01–0.02 mg/kg, IV) or *glycopyrrolate* (0.002–0.005 mg/kg, IV) for treating bradycardia.
  –   *Methoxamine* or *phenylephrine* to treat decreased vascular resistance.
  –   *Calcium gluconate* (10–20 mg/kg, IV infused slowly) to counteract hyperkalemia-induced dysrhythmias and/or to support blood pressure.
  –   *Lidocaine* (1–2 mg/kg, IV) for ventricular dysrhythmias (premature contractions and tachycardia).
o   *Bicarbonate* (0.5 mEq/kg, IV) is recommended when resuscitation is prolonged.
  –   Administration is ideally based on acid–base status.

E. **Defibrillation**

o   Indicated for ventricular fibrillation, but may only be practical in *foals*.
  –   Unlikely to be successful in the adult horse.
o   Dose: 2–4 joules/kg.

Postoperative myopathy

- A number of different types of *degenerative* myopathies occur in the horse.
- Causes include:
  - *Genetic* defects in muscle fibers.
  - *Nutritional* disorders (e.g. deficiencies in selenium and vitamin E).
  - *Inherited* disorders (e.g. polysaccharide storage disease, hyperkalemic periodic paralysis).
- These myopathies may be exacerbated by the stress of surgery and anesthesia.

I. Postoperative myopathy

- Refers to ischemic muscle damage which occurs in the anesthetized horse.
- More likely to occur in *bigger* horses and during *prolonged* anesthesia.
- Although the problem starts during the period of anesthesia, clinical signs of myopathy usually do not become evident until the horse attempts to stand.
- Postoperative myopathy appears to be less common nowadays and this may be the result of a better understanding of the contributing factors.

A. Compartmental syndrome

- A term used to describe local muscle ischemia, and subsequent muscle contracture, resulting from edema and increased pressure within osteofascial compartments.

B. Crush syndrome

- Uncommon in horses.
- It describes the systemic manifestations of muscle necrosis including:
  - Shock.
  - Renal failure from myoglobinuria.
  - Cardiac events subsequent to metabolic acidosis and hyperkalemia.

II. Clinical signs

- Are dependent on the severity of the condition and the location of the muscle damage.
- Are generally noticed when the horse attempts to stand.
  - Mild cases may not be noticed until the horse is walking.
- The condition usually occurs in *dependent* muscles; however, *nondependent* muscles may be affected.
- Signs include:
  - Difficulty in recovery due to inability to bear full weight on affected limb(s).
  - Lameness (mild to severe).
  - Localized swelling and varying degrees of hardness of muscle(s).
  - Sweating (due to pain) may be severe.

○   Muscle fasciculations may be present.
○   Myoglobinuria.

Comment: It may sometimes be difficult to differentiate triceps myopathy from radial nerve damage. Usually with *radial nerve* injury there is no muscle swelling or pain; however, it is possible that both conditions may co-exist in some cases.

III. Contributing factors

- Large body mass of horse.
- Long duration of recumbency.
- Inadequate padding of body and support of limbs.
- Improper positioning (e.g. horse tilted to one side while in dorsal recumbency).
- Intraoperative hypotension.
- Hypoxemia.

IV. Pathogenesis

A. Ischemic injury

○   Is thought to be the initiating factor in postoperative myopathy.
○   The increase in dependent muscle pressure in the recumbent horse is such that muscle perfusion is diminished to the extent that capillary damage results.

B. Decreased perfusion

○   Leads to ischemia of muscle capillaries which, in turn, leads to increased permeability of the capillary walls and *edema* formation.
○   Edema perpetuates the increase in compartmental pressure (within muscle fascia).
○   Unless the arterial flow can be restored (e.g. by repositioning horse) in a timely manner and before a 'critical' pressure develops, serious consequences for the muscle may result.

C. Reperfusion of ischemic muscle

○   Characterized by:
  –   Decreased O_2 utilization.
  –   Decreased blood flow.
  –   Increased vascular tone.

D. Non-dependent limb myopathy

○   The development of myopathy in a *non-dependent* limb would not appear to fit into this model of ischemia, but vascular compromise is likely to be the root cause here also.

V. Factors influencing muscle blood flow

A. Systemic blood pressure

○ Maintain blood pressure > 75 mmHg in adult.
  –   Hypotension is linked to myopathy in horses.

B. Intracompartmental muscle pressure

○ Is a function of:
  –   Duration of pressure increase.
  –   Metabolic rate of tissues.
  –   Vascular tone.
  –   Local blood pressure.
  –   Venous drainage.
  –   Surface pressure on the muscle compartment (affected by padding and mass of horse).

VI. Reducing the incidence of postanesthetic myopathy

● Decrease the duration of recumbency.
● Provide adequate padding.
● Position the horse properly (see Chapter 13):
  ○ Place horse squarely on its back when in dorsal recumbency.
  ○ Avoid extreme flexion or extension of limbs.
  ○ Position upper limbs parallel to table when horse is in lateral.
  ○ Do not place support padding on top of the lower limb in an effort to support the upper limb, as this may affect venous drainage of lower limb.
● Avoid intraoperative hypotension.
  ○ Maintain mean arterial pressure > 75 mmHg in adult.

VII. Sequelae

● Injury (e.g. long bone fracture) in the recovery period due to incoordination and weakness.
● Renal damage from myoglobinuria.
● Muscle wasting (may be chronic).

VIII. Treatment

● Some horses may need assistance to stand during and following recovery.
● If the horse is recumbent, provide adequate padding and nursing care.
● Mild cases should benefit from light exercise (i.e. walking), starting on the day following recovery from anesthesia.

- Maintain hydration.
  - However, infusions of large volumes of isotonic fluid may be detrimental as this may increase intracompartmental pressure.
- *Mannitol* has been shown, in experimental models of ischemic myopathy, to reduce intracompartmental pressure and improve tissue oxygenation.
  - It may also provide protection against myoglobin-induced renal tubular damage.
  - A bolus of *mannitol* (0.25 g/kg, IV) may be repeated two or three times in the first 24 hours.
- Provide analgesia.
  - NSAIDs should suffice in mild cases.
  - More severe cases require more intensive analgesia.
- Provide *vitamin E* and *selenium*, if deemed to be deficient.
- Another treatment that has been recommended is *DMSO*.
- Local treatment of affected muscle (e.g. various massage modalities, ultrasound therapy) has been recommended.

Neuropathy

- Anesthesia-related nervous system injuries occur in the horse.
  - Most commonly, the insult involves *peripheral nerves* (e.g. radial, facial).
  - On rare occasions it may involve the *spinal cord*.
- Many of the factors involved in the development of postanesthetic myopathy are also important in the development of neuropathy.
- Clinical signs:
  - Are dependent on the severity of the condition and the location of the nerve damage.
  - Are generally noticed when the horse attempts to stand.
    - Mild cases may not be noticed until the horse attempts to walk.
- The condition usually occurs in *dependent* nerves; however, *nondependent* nerves may be affected.

I. Contributing factors

- Large body mass of horse.
- Long duration of recumbency.
- Inadequate padding of body and support of limbs.
  - Direct pressure from hard surface or object (e.g. a halter buckle causing *facial nerve* damage).
- Improper positioning.
  - The lower thoracic limb should be pulled forward to release the triceps muscle and radial nerve from under the thoracic cage.
  - If *radial nerve* damage has occurred in the *non-dependent* limb it may be that the brachial plexus has been damaged by malposition of the limb.
- Overextension of limbs.
  - For example, *femoral nerve* paralysis may result from overextension of the pelvic limbs when the horse is in dorsal recumbency.

II. Radial nerve injury

A. Clinical signs

- o Vary with the severity of the injury.
- o Signs may be evident when the horse attempts to stand or may not develop for some hours after recovery.
  - – It is not always easy to differentiate radial nerve damage from triceps myopathy.
- o Inability to bear weight on affected forelimb.
- o Elbow is 'dropped' due to lack of triceps tone.
- o Inability to extend the thoracic limb.
- o Generally no pain in affected area unless triceps myopathy co-exists.
- o In cases where the onset of clinical signs of radial nerve damage is *delayed*, it is likely that the nerve damage occurred from swelling of the triceps as a result of myopathy.

B. Sequelae

- o Difficult recovery from anesthesia.

C. Outcome

- o Most cases regain neurological function in a few days.
- o Permanent nerve damage results in some cases.

III. Femoral nerve injury

- • Probably results from overextension of the pelvic limbs with the horse in dorsal recumbency.

A. Clinical signs

- o May involve one or both pelvic limbs.
- o Inability to stand if both pelvic limbs are involved.
- o Inability to *extend* the stifle.
- o *Flexion* of hock is evident.
- o Usually no swelling of muscles in pelvic limb, unless myopathy coexists.

B. Sequelae

- o Difficult recovery or unable to stand.
- o Further injury (e.g. long bone fracture) likely to result if horse makes repeated attempts to stand.
- o Mild cases should resolve in a few days.

IV. Peroneal nerve injury

- Uncommon occurrence.
- Usually occurs in *dependent* limb with the horse in lateral recumbency.

A. Clinical signs

- ○   Horse is usually able to stand.
- ○   Inability to *flex* the hock and *extend* the foot.

B. Sequelae

- ○   Mild cases should resolve in a few days.

V. Facial nerve injury

- Usually results from the *halter buckle* applying pressure over the nerve with the horse in lateral.

A. Clinical signs

- ○   Motor paralysis of facial muscles.
- ○   Drooping of lip is most common sign.

B. Sequelae

- ○   Mild cases resolve in a few days.
- ○   Condition may be permanent in some cases.

VI. Spinal cord myelomalacia

- Has been described following anesthesia in horses.
- Horses are usually young and often of the heavier breeds.
- The condition is thought to be ischemic in origin and may be associated with low arterial pressure or fibrocartilaginous emboli.

A. Clinical signs

- ○   Pelvic limbs are involved and the horse is unable to stand.
- ○   Horse may 'dog-sit' or adapt Schiff–Sherrington posture.
- ○   Loss of deep pain perception.
- ○   Lesion is usually in *thoracolumbar* region of cord.
- ○   Horse does not seem to be in pain.

B. **Sequelae**

     o   Little chance of recovery.

VII. Myelogram-associated neuropathy

- Myelograms generally cause deterioration in neurological function in the postanesthetic period.
- It is common for horses to show an increased neurological deficit (usually one grade change) for a few days after a myelogram.
- Prior administration of NSAIDs may lessen the effects of the myelogram.
- On rare occasions, horses may have temporary *blindness*.

VIII. Cerebral cortical necrosis

- Signs of cerebral cortical injury have been reported to develop within a few hours of recovery from anesthesia or up to 7 days later.
- May be linked to cerebral ischemia during the anesthesia period.

A. **Clinical signs**

     o   Blindness.
     o   Behavioral disturbances such as:
         – Compulsive pacing.
         – Head pressing.
         – Lethargy.
         – Seizures.

B. **Sequelae**

     o   Recovery is unlikely.

IX. Treatment of peripheral neuropathies

- Treatment of peripheral neuropathies is very similar to treatment of myopathies and is mainly supportive.
- Some horses may need assistance to stand during and following recovery.
  - o   Consider using a *sling* if the horse has difficulty in standing.
- If recumbent, provide adequate padding and nursing care.
- Maintain hydration.
- Anti-inflammatories (e.g. NSAIDs).
  - o   NSAIDs will also provide analgesia if there is associated myopathy.
- Another recommended treatment is DMSO.
- Local treatment of affected area, including various massage modalities and ultrasound therapy, has been recommended.

Hyperkalemic periodic paralysis

Rachael E. Carpenter

- Hyperkalemic periodic paralysis (HYPP) has been estimated to occur in 0.4% of American Quarter Horses and 2% of registered Quarter Horses.
  - HYPP is most often seen in young, heavily muscled Quarter Horses that are used as halter show horses.
  - Heavily muscled Quarter Horse foals presenting with upper airway stridor or discharge of milk from the nares should have HYPP as a differential diagnosis.
- It also occurs in Quarter Horse crosses, Appaloosas, and American Paint horses.
- Careful anesthetic management of horses affected by HYPP is important to ensure a positive outcome in the perioperative period.

I. Clinical signs

- These include:
  - Muscle fasciculations and weakness which may lead to 'dog-sitting' or recumbency.
  - Other clinical signs include prolapse of the nictitating membrane, facial muscle spasm, and sweating.
  - *During anesthesia*, clinical signs may include:
    - Prolonged recovery (the most common complication).
    - Muscle fasciculations.
    - ECG changes.
    - Tachycardia.
    - Tachypnea.
    - Hypercapnia.
    - Hyperthermia.
  - *Foals* may have spasm or paralysis of the pharyngeal and laryngeal muscles.
    - Increased respiratory noise and milk discharge from the nares may be present.
- Often these episodes may be confused with colic, laminitis, exertional rhabdomyolysis, or cardiac or neurologic disease.
- Clinical episodes may last from a few minutes to a few hours and often resolve without medical intervention.
- Rare cases may be *fatal* because of cardiac or respiratory failure.
- Not all affected horses show clinical signs.
  - A variety of stressors (e.g. cold weather, diet change, transport, unaccustomed physical exertion, illness) may trigger an episode.

II. Pathogenesis

A. Inherited as an autosomal dominant trait

- Affected horses are descendants of the Quarter Horse sire, *Impressive*.
- Horses *homozygous* for HYPP are more severely affected than heterozygotes.
- Males are more commonly affected, but the trait is not thought to be sex-linked.

B. **Genetic defect in the sodium–potassium pump**

o HYPP is caused by a genetic defect in the Na–K pump that renders the cell membrane excessively permeable to sodium.
o The cell membrane is normally more permeable to potassium than sodium.
o In HYPP patients, a defective population of the sodium channels fails to inactivate allowing excessive inward sodium current.
  – In addition, these defective sodium channels will open in response to an increase in serum K concentration.
o Failure to close the sodium channels leads to partial depolarization of the cell and a less negative resting membrane potential.
o Reduction in membrane potential may cause further opening of these sodium channels, full depolarization of the cells, and *uncontrolled muscle activity*.

C. **Hyperkalemia**

o Is thought to result from cellular leakage during uncontrolled muscle contractions.
o During episodes of HYPP, the serum K is usually increased above baseline values and may remain so for 1–2 hours.

D. **Normokalemic variant**

o A normokalemic variant of HYPP has been described in a small number of horses.

III. Diagnosis

A. **Polymerase chain reaction**

o Currently the preferred test.
o Is the most sensitive and specific test for HYPP.
  – It is currently being performed at the University of California at Davis Veterinary Genetics Laboratory using a whole *blood or hair* sample from a live horse or tissue samples from necropsy specimens.

B. **Electromyography (EMG)**

o Can be used to *screen* and *diagnose* HYPP.
o Abnormal EMG signals can be found during or between episodes.
  – Affected horses will have spontaneous activity that will include high-frequency myotonic discharges and trains of doublets.
    ■ Myotonic discharges and doublets have been reported to be 90% sensitive and specific for HYPP in descendants of Impressive.
  – Other abnormal findings may include prolonged insertional activity, fibrillation potentials and positive sharp waves.

C. **Potassium challenge test**

- o   May be used to *confirm a diagnosis* of HYPP.
- o   *This test is **not** commonly used due to the risk of adverse reaction or death.*
- o   Horses are fasted for 12 hours and then given an initial dose of KCl (88–160 mg/kg diluted in 6 liters of water) via a nasogastric tube.
    - –   Affected horses usually exhibit clinical signs 1–3 hours after administration, and serum K concentrations increase significantly over baseline values.
    - –   The amount of K used in the test is too low to cause a problem in normal horses, but will often trigger an episode in horses that have abnormal resting membrane potentials.
- o   A *positive diagnosis* is made when hyperkalemia occurs and continuous muscle fasciculation at several sites is evident.
- o   This test may give *false negative* results and must be repeated.

IV. Perioperative preparation and treatment

A. **Owner education**

- o   In surgical cases, the potential for anesthetic complications associated with HYPP should be discussed with the owner prior to any anesthetic event.
    - –   Stress induced by fasting and anesthesia reportedly increases the risk of HYPP episodes in susceptible horses.
- o   Dietary change may also precipitate attacks.

B. **Evaluation of the patient**

- o   As with all horses undergoing general anesthesia, a thorough *history* and *physical examination* should be performed.
- o   Electrocardiogram, complete blood count and serum chemistry are recommended in suspected HYPP cases.

C. **Drugs used in perioperative management of HYPP**

- o   Proper sedation should be given to potentially affected foals when undergoing examination or anesthesia as the associated stress (e.g. from restraint) can precipitate an episode.
- o   A variety of drugs may be used in the perioperative management of HYPP (see Table 21.1) to manage HYPP horses.

D. **Drugs with potential to exacerbate HYPP**

- o   Depolarizing neuromuscular blockers cause slight increases in serum K and should be avoided.
- o   *Potassium penicillin* has 1.6 mEq of potassium/million units which does not increase serum [K] in normal horses, but may precipitate an attack in susceptible horses.
- o   Potassium-sparing diuretics (e.g. *spironolactone*, *amiloride*) reduce urinary excretion of potassium and increase serum [K].

Table 21.1   Drugs used in perioperative management of HYPP in horses.

Agent	Dose	Comments
Acetazolamide	2.2 mg/kg, orally; q8–12 h	Potassium-wasting diuretic; may be given for at least 2 days prior to elective surgery
Hydrochlorothiazide	0.5–1 mg/kg, orally q12 h; or 1 mg/kg IV	Alternative to acetazolamide to reduce potassium load prior to elective procedures
Calcium gluconate (23%)	0.2–0.4 ml/kg IV	Should be given slowly; cardioprotective, so other methods to decrease serum K^+ should be started simultaneously
Sodium bicarbonate	1–2 mEq/kg IV	Should be given slowly over 15–20 min; alkalinizing, moves potassium intracellularly
Dextrose (50%)	0.25–0.5 ml/kg IV	Stimulates the release of insulin and promotes uptake of potassium by the cells
Insulin	0.055 IU/kg	Dosage not well established in horses; monitor blood glucose to prevent hypoglycemia

- NSAIDs have the potential to increase serum [K], although controlled studies have not supported this.
- *Ketamine* causes increased muscle tone and rigidity, and some clinicians have warned against its use in HYPP patients.
- There are reports of HYPP episodes occurring with *halothane* and *isoflurane*.
  – The potential for a HYPP episode exists with any volatile anesthetic.

E. Preoperative diuretic therapy

- Therapy of HYPP horses undergoing elective surgery usually includes diuretic therapy for at least 2 days prior to surgery to reduce potassium.
- Oral *acetazolamide* (2.2 mg/kg every 8–12 hours) or thiazide diuretics (*hydrochlorothiazide* 0.5–1.0 mg/kg, orally every 12 hours or 1 mg/kg, IV) are most commonly recommended.
  – It is not clear whether IV *acetazolamide* is effective during acute attacks.

F. Pre-anesthetic sedation

- Essential in reducing stress of horses with HYPP.
- Pre-anesthetic sedation with up to 0.8 mg/kg *xylazine* IV and quiet handling will reduce stress and calm the patient in the immediate perioperative period.
  – The choice of a specific agent is probably less important than reducing overall stress in these patients.

G. Fluid therapy

- Fluids should be given continuously during anesthesia.
  – *Potassium-free fluids* are recommended (e.g. 0.9% NaCl).

○   If an episode occurs during anesthesia, diuresis should be instituted to dilute the high serum K.

V. Intraoperative therapy

- *Calcium gluconate* (23%, 0.2 to 0.4 ml/kg, IV) is recommended for acute episodes of HYPP during anesthesia.
  - ○   *Calcium gluconate* protects against the cardiotoxic effects of hyperkalemia and prevents arrhythmias.
  - ○   Because administration of calcium does not address the hyperkalemia, methods to *lower* serum K should be implemented concurrently.
- Treat acidemia.
  - ○   Acidemia causes extracellular shifting of K that may be detrimental.
    - –   If a HYPP episode occurs under anesthesia, alkalinizing the blood will promote potassium influx intracellularly.
    - –   Administer *sodium bicarbonate* ($NaHCO_3$) (1–2 mEq/kg, IV).
    - –   Prevent respiratory acidosis by the use of *controlled ventilation*.
- *Dextrose* promotes release of insulin and promotes uptake of K by the cells.
  - ○   *Dextrose* (0.25–0.5 ml/kg of 50% *dextrose*) has been advocated in the treatment of hyperkalemia.
- *Insulin* has been advocated for shifting K into the cells, but the appropriate dosage is not well established in horses.
  - ○   Subcutaneous *NPH insulin* (0.055 IU/kg) has been recommended.

VI. Intraoperative monitoring

- Blood gases, glucose, and serum electrolytes should be measured periodically.
  - ○   Every effort should be made to maintain blood pH at or near normal values.
  - ○   Serum K should be closely monitored.
- ECG monitoring is essential to detect cardiac effects of hyperkalemia.
  - ○   ECG changes are often the first signs of HYPP during anesthesia.
  - ○   These changes include (see Figs 21.1a and 21.1b):
    - –   Increasing amplitude of T waves.
    - –   Bradycardia.
    - –   Decreasing amplitude of P waves
    - –   Widening of QRS complexes.

Fig. 21.1a   Normal ECG of an HYPP susceptible horse under anesthesia. Serum potassium was 3.75 mmol/liter (normal 2.3–5.1 mmol/liter). Reprinted with permission from *Journal of the American Veterinary Medicine Association* **226**: 875; 2005.

Fig. 21.1b   ECG of the above horse later during anesthesia showing changes characteristic of hyperkalemia (serum potassium 7.49 mmol/liter). Note the decreased amplitude of the P waves and increased amplitude of the T waves. Reprinted with permission from *Journal of the American Veterinary Medicine Association* **226**: 875; 2005.

VII. Recovery

- Horses should recover in a quiet, darkened, padded stall with oxygen supplementation.
  - To minimize stress, *xylazine* may be given (0.1–0.2 mg/kg, IV).
  - Analgesics may also be given to smooth recovery.
- *Prolonged recovery* is the most common complication from general anesthesia of HYPP patients.
  - In these cases, arterial blood gas, acid–base status and serum potassium concentration should be measured and treated as necessary.
- Other reported difficulties include:
  - Dyspnea on extubation.
  - Collapse after anesthesia.
  - Muscle fasciculation.

Equine malignant hyperthermia

Rachael E. Carpenter

- Malignant hyperthermia (MH) is a clinical syndrome that occurs in humans, pigs, dogs, cats, and horses.
- It is most commonly elicited as a response to known anesthetic triggers, making anesthetic management challenging in these patients.
  - Other triggers may include stress, exposure to cold, exercise, or sympathetic nervous system stimulation.

I. Signalment and signs

A. Incidence in the horse

- Based on the number of case reports in the literature, the incidence of MH in horses appears to be low.
  - There is the possibility of under-diagnosis and under-recognition of MH due to the overlap in clinical signs between MH and other muscle disorders.

B. Breeds reported to be affected

- o Quarter Horses.
- o Thoroughbreds.
- o Appaloosas.
- o Arabians.
- o Ponies.

C. Clinical signs

- o Hypercarbia.
  - – Often, an increase in end-tidal carbon dioxide ($ETCO_2$) despite constant minute ventilation is the *earliest sign*.
- o Skeletal muscle rigidity.
- o Tachypnea.
- o Rapid increase of core body temperature.
  - – Often occurs *late* in an MH episode.
- o Severe metabolic acidosis.
- o Cardiac arrhythmias.
- o Serum K and creatine kinase (CK) concentrations are increased during the anesthesia and post-anesthesia period.

Comments:
- o Unlike pigs, but similar to the syndrome reported in humans and dogs, horses may not show signs of MH until after 3 or more hours of anesthesia.
- o Clinical signs of MH in horses may be subtle and easily missed unless physiologic monitoring (e.g. $ETCO_2$) is available.
- o If left untreated, MH will invariably lead to death.

D. Differential diagnoses

- o Other muscle disorders (e.g. HYPP, exertional rhabdomyolysis) may show similar clinical signs and laboratory abnormalities, including increased $PaCO_2$, electrolyte abnormalities, increased or decreased muscle tone, and hyperthermia.
- o Chronic rhabdomyolysis has been described as a non-anesthetic manifestation of MH in humans.

II. Pathogenesis

- MH episodes are a result of uncontrolled intracellular Ca^{2+} release from the sarcoplasmic reticulum of skeletal muscle into the myoplasm, in the presence of halogenated volatile anesthetics and depolarizing muscle relaxants.
- Unopposed muscle contracture, release of cations and enzymes (e.g. CK) into the circulation, and production of heat and acid can be traced to pathological increases of intracytoplasmic calcium.
- Two main channels for Ca^{2+} movement are important for the normal excitation–contraction coupling process:

○   The voltage-gated *dihydropyridine receptor* (CACNA1S).
– In humans, more than 60 mutations in the RyR1 gene and six mutations in CACNA1S are associated with MH.
○   The *ryanodine receptor* (RyR1).
– Recent work in horses has determined that a mutation in the RyR1 gene is associated with MH.

III. Diagnosis

●   Most commonly, MH events occur in healthy animals with *no previous history* of anesthetic problems and no advance warning.
●   A presumptive diagnosis of MH sensitivity should be made if a close relative of the animal has had a reaction compatible with MH during anesthesia.
●   *Avoidance of trigger agents* may be the most cost-effective manner of dealing with suspected MH cases.

A. Contracture response

○   In porcines, muscle physiology studies revealed a difference in contracture responses to *caffeine* and *halothane* in MH-positive individuals when compared with normal individuals.
○   This *in vitro contracture testing* (IVCT) has become a routine technique in establishing the diagnosis of MH in affected species.

B. Polymerase chain reaction (PCR)

○   In porcines, reliable PCR techniques have been developed to detect porcine MH and identify affected and carrier animals.
○   Recent discovery of a specific mutation in the RyR1 gene associated with MH in horses may make PCR testing possible in this species.

C. In vitro contracture testing (IVCT)

○   IVCT may be performed on horses with suspected MH; however, a negative contracture test *does not* exclude MH.
○   The test is performed at only a few regional centers in the US and Canada, and may be cost-prohibitive to many owners.

D. Clinical signs during anesthesia

○   During anesthesia, clinical diagnosis of MH has classically required at least three of the following signs:
– Cardiac arrhythmias.
– Acidemia.
– Hypercarbia.
– Increased body temperature.
– Muscle rigidity.

      o   Persistent increases in $ETCO_2$ despite intensive positive pressure ventilation (PPV) should prompt the inclusion of MH high on a list of differentials.

IV. Preoperative preparation

A. History and physical examination

      o   As with all patients undergoing general anesthesia, a thorough history and physical examination should be performed.

B. Avoid known triggers

      o   In suspected or documented cases of MH, avoiding known anesthetic triggers is the most important aspect of anesthetic management.
          –   Anesthetic agents to avoid include all volatile anesthetics and depolarizing neuro-muscular blocking drugs (i.e. *succinylcholine*).

C. Anesthetic agents

      o   Safe anesthetic agents include all drugs in the following groups: benzodiazepines, phenothiazines, barbiturates, *etomidate*, *propofol*, dissociative agents, opioids, *nitrous oxide*, nondepolarizing neuromuscular blockers, and local anesthetics.
      o   Alpha$_2$ agonists have not been specifically studied, but are believed to be safe.
      o   *Guaiphenesin* has not been reported to be either a safe or a triggering agent.
      o   Without sufficient tranquilization and muscle relaxation, *ketamine* and high doses of opioids may be contraindicated because of the muscle rigidity and excitement that can be associated with these agents.

D. Effects of preanesthetic stress

      o   Preanesthetic exertion, psychological stress, and sympathetic nervous stimulation have been shown to enhance MH reactions.
          –   Therefore, preanesthetic stress should be minimized (e.g. with sedatives and analgesics).

E. Induction of anesthesia

      o   Can be accomplished with standard intravenous agents.

F. Maintenance of anesthesia

      o   Total intravenous anesthesia is a good choice. (See Chapter 15 – TIVA.)

G. Regional/local anesthetic techniques

      o   Can be used safely in patients with MH.

○ The stress of excessive physical restraint could be sufficient to initiate an MH reaction, so adequate sedation in conjunction with regional/local techniques is important.

H. Ventilation and oxygenation

○ Whenever an MH-positive horse is anesthetized, ventilatory support and oxygen administration should be instituted.

V. Treatment

A. Discontinue triggering factor(s)

○ The most important step in effective treatment of an MH event.
○ The anesthetic machine should be changed to one that is not contaminated with volatile agents or flushed with 100% O_2 to remove residual anesthetic.
  – Alternately, O_2 and PPV can be administered with a demand valve.
○ Positive pressure ventilation with 100% O_2 should be instituted or continued.
○ Check arterial blood gases, CK, blood glucose, serum lactate, and electrolytes.

B. Dantrolene

○ The only reliable and specific therapeutic agent for MH.
○ Is an intracellular calcium antagonist and skeletal muscle relaxant.
○ The dosage is 2–3 mg/kg IV (up to 10 mg/kg, IV) depending on severity of clinical signs and response to treatment.
  – Few veterinary hospitals stock *dantrolene*, but it may be wise to have it available when suspected or positive MH horses are scheduled for elective procedures.
  – The commercial parenteral preparation may be cost prohibitive in equine patients (approximately $1500 for 500 mg), but a method has been described for using the oral preparation intravenously.

Prophylactic use
○ There is no evidence that prophylactic *dantrolene* is beneficial.
  – In one case report it was suspected as the cause of prolonged postoperative recumbency in a Clydesdale.

C. Cardiac arrhythmias

○ Arrhythmias resulting from hyperkalemia are thought to be the most common cause of death from MH.
  – Intravenous fluids should be administered for diuresis, and *sodium bicarbonate* (1–2 mEq/kg, IV) and 50% *dextrose* (0.25–0.5 ml/kg, IV) may be administered to correct acidemia and hyperkalemia.
  – Treatment for hyperkalemia usually includes calcium as a cardioprotectant, but it is *not recommended* when the hyperkalemia is a result of MH.
○ *Lidocaine* or *procainamide* (1–2 mg/kg boluses, IV) should be available to treat premature ventricular contractions or ventricular tachycardias.

D. Hyperthermia

o   If the horse is hyperthermic, ice and cold water (or alcohol) should be applied to the body surface in areas of high blood flow (e.g. jugular grooves, inguinal, axillary regions).

o   Cooled fluids and cold-water enemas may help to reduce core temperature.

o   If the surgical procedure involves a body cavity, iced-fluid lavage could be performed, but the priority should be completion of the procedure.

Comment: Cooling is *controversial* because it promotes peripheral vasoconstriction and may delay entry of *dantrolene* into skeletal muscle.

E. Nondepolarizing muscle relaxants

o   Nondepolarizing muscle relaxants block acetylcholine from occupying binding sites at the neuromuscular junction and therefore prevent muscle depolarization and contraction.

o   While nondepolarizing muscle relaxants have not been shown to be curative in MH, they may be beneficial in cases where *dantrolene* is unavailable.

VI. Intraoperative monitoring and recovery

A. Monitor $ETCO_2$

o   Increases in $ETCO_2$ are frequently the first signs of an MH reaction, so an $ETCO_2$ monitor should be used in patients with suspected or confirmed MH.

o   If $ETCO_2$ monitoring is not available, arterial blood gas samples should be monitored periodically.

B. Further intraoperative monitoring

o   Direct blood pressure.
o   Heart and respiratory rates.
o   ECG.
o   Core body temperature.

C. Duration of monitoring

o   Monitoring is recommended for 24–48 hours postoperatively to ensure that the initial MH event has been appropriately treated and does not reoccur.

D. Prognosis

o   After appropriate treatment of an MH event, the patient should be able to return to normal activities and live a normal quality of life.

Delayed awakening

- Excessively delayed recovery from anesthesia is unusual in healthy adult horses.
- Prolonged recoveries (up to 2 hours) are not uncommon following emergency intestinal surgery.
  - This may be a result of these horses becoming fatigued from the colic episode.
  - In general, they make an uneventful recovery.
- Prolonged recovery is more likely to occur in foals due to hypothermia and or hypoglycemia after a long surgery.

I. Sedatives

- Pre- or postoperative administration of sedatives or tranquilizers (e.g. *acepromazine*) will prolong recovery, though usually not excessively.
- Long-acting sedatives/tranquilizers should not be given to neonatal foals.

II. Anesthetic drugs

- Long-acting intravenous drugs (e.g. *pentobarbital*) will contribute to prolonged recoveries.
- Recovery is a little longer with the more lipid-soluble inhalation anesthetics (e.g. *halothane*) than with the less soluble anesthetics (e.g. *sevoflurane*).

III. Anesthesia-associated pathological changes

- The following may contribute to prolonged recoveries:
  - Hypoxia.
  - Hypotension.
  - Acid–base abnormality.
  - Hypothermia (more likely to be a problem in foals and miniature horses).
  - Hypoglycemia (more likely to be a problem in neonates).

IV. Surgically induced pathological changes

- The following may cause prolonged recoveries:
  - Embolus lodging in the central nervous system.
  - Bleeding from surgical site leading to hypotension and shock.

22   Assisted recovery

Bernd Driessen

I. Recovery-associated problems

- Despite the progress in equine anesthesia, recovery from general anesthesia remains a potentially life-threatening event for the horse and a challenge for the anesthetist, even when anesthetic and surgical management is routine.
  - In large part this is due to the horse's *flight behavior* prompting the animal to stand prematurely (i.e. before anesthetic agents and their depressant effects on mental, proprioceptive, and motor function have worn off).
- Based on previous enquiries into perioperative morbidity and mortality, anesthesia-related complications are especially high in the horse, with fatality rates reaching on average 1% for elective equine surgeries and rising to overall 4–8% when emergency procedures are also considered.
  - Injuries to the musculoskeletal apparatus (fracture, myopathy) rank among the top three complications associated with perioperative death.
  - Contributing factors include:
    - Intra- and postoperative cardiopulmonary complications.
    - Postoperative pain.
    - Type of surgical procedure, with fracture repair carrying the highest risk.
    - Prolonged anesthesia.
- An appropriate environment (i.e. an adequately designed recovery stall) is a prerequisite to avoid injuries in the postoperative period.
  - Additional techniques aimed at assisting the horse while recovering from anesthesia should be considered.
  - However, none of the described methods of assisted recovery has completely eliminated the risk of severe or even fatal postanesthetic complications.

II. Recovery stalls

A. Structural features designed to optimize conditions for recovery

- Close proximity to, but separate from, surgery room.
- Area: 4–5 m^2 (~ 43–54 ft^2) for average-sized adult horses.
  - Avoid oversized stalls.
- Well padded walls and doors at least 2.5–3.0 m (~ 8–10 ft) high.
- Soft floor with non-slip surface (even when wet).
- Front and back doors locked by transverse bars and floor/ceiling bolts.
- Holes placed high in doors allowing head and tail ropes to be passed to the outside.
- Heating/air-conditioning system allowing for separate climate control within recovery stall.
- Light source equipped with dimmer function.

B. **Useful design features for various methods of assisted recovery**
- o Door windows, cameras, or observation platform to allow monitoring of the horse.
- o Recessed wall outlets for oxygen supply, suction lines, and electrical power.
- o Stout metal rings recessed into the wall of each corner, well above a horse's head height (~ 2.5 m or 8 ft above floor).
- o Ceiling hook centered over the stall to hold a hoist.
  - – Alternatively, overhead monorail with hoist.
- o Escape route for personnel attending the horse within the stall during recovery.
- o Movable 30–40 cm (12–16 inch) thick, vinyl-covered, foam mattress.

III. Prerecovery preparation

- • The horse, being a flight animal, tends to attempt escape from any 'adverse condition' that frightens or hurts it, often leading to premature and violent attempts to stand when awakening.

A. **Guidelines for planning a successful recovery** (see Table 22.1)
- o Ideally, planning for the recovery phase should begin early.
- o The aim is to improve the quality of recovery by:
  - – Rendering the patient calm (administration of sedatives).
  - – Reducing pain.
  - – Allowing more time for residual anesthetics to be eliminated from the body.

Table 22.1 Drugs commonly used for pre-recovery sedation and analgesia.

Drug	Dose for intravenous (IV) administration	Indication
α_2 agonists		To produce calming and analgesia
Xylazine	0.1–0.2 mg/kg	Prolong sleeping phase
Detomidine	2–4 µg/kg alone or followed by CRI of 0.1–0.6 µg/kg/min	Delay initial attempts to rise
Medetomidine	1–2 µg/kg alone or followed by CRI of 0.03–0.06 µg/kg/min	
Romifidine	8 µg/kg	
Acepromazine	5–15 µg/kg	Reduces excitement
		Reduces risk of hypertension with α_2-agonist administration
		Inhibits opioid-induced excitement
Propofol	2 mg/kg	Prolongs sleeping phase
Opioids		Provide short-term pain relief
Butorphanol	0.01–0.02 mg/kg alone or followed by CRI of 24 µg/kg/h	Prolong sedative action of α_2-agonists
Pethidine	2.0 mg/kg (IM)	
Non-steroidal drugs		Provide relief of musculoskeletal pain
Flunixin meglumine	1 mg/kg	Reduce inflammation
Phenylbutazone	4 mg/kg	

B. **Provide analgesia**

○ Analgesia should be used prior to or during surgery, to provide pain relief that lasts into the postanesthetic period.
○ One or a combination of the following techniques can be used:
– Systemic, regional, or spinal/epidural administration of local anesthetics.
– Systemic, spinal/epidural, or intra-articular administration of opioids.
– Systemic or spinal/epidural administration of α_2 agonists.
– Systemic administration of anti-inflammatory drugs (NSAIDs).

C. **Place the horse on a thick mattress**

○ Helps delay first attempts to stand by increasing the horse's comfort.
○ Necessary if *pre-recovery* treatment with sedatives/tranquilizers is likely to significantly prolong recumbency.
○ Helps to avoid pressure injuries to neuronal and musculoskeletal structures.

D. **Ensure adequate oxygenation**

○ Ensure *a patent airway* and adequate *blood oxygenation*.
– Hypoxemia rapidly induces muscle fatigue and causes restlessness, both of which compromise the horse's ability to stand safely.
– Leave the horse orally or nasally intubated throughout the recovery period or at least until the horse is actively swallowing.
– Provide supplemental oxygen if necessary.

E. **Empty urinary bladder**

○ Depending on length of anesthesia and the type and volume of pre- and intraoperatively administered fluids and drugs administered, it might be necessary to empty the horse's bladder as a full bladder leads to restlessness.
– Urination will lead to a slippery recovery-stall floor.

F. **Protect extremities and head from injury**

○ Padded bandages on legs to prevent additional trauma.
○ Leather helmets or plastic hoods to protect surgery sites in the head.

IV. **Methods of assisted recovery**

● A broad variety of options ranging from simple methods to very sophisticated systems can be used to assist horses recovering from anesthesia. (See Table 22.2.)
● Many factors have to be considered when selecting the appropriate recovery system for an individual patient. (See Table 22.3.)

Table 22.2 Common techniques of assisted recovery in the horse.

Method of assisted recovery	Group of horses for which technique is suitable	Advantages	Disadvantages/Complications
Personnel within recovery stall assisting patient manually	General patient population Well tempered horses Small equines (foals, ponies)	No extra equipment needed; patients are closely monitored	Potentially dangerous for attendants Requires trained personnel
Head and tail rope recovery	General patient population nervous or excited horses Not well trained horses Horses undergoing prolonged anesthesia Horses with muscle weakness Mild to moderate neurological deficits	Better protection of attendants than 'hand-recovery' Allows for more than two attendants to help	Requires wall rings and/or holes in recovery-stall doors Loss of head or tail rope when head or tail rope attachment/knot fails Horse fighting head restraint Requires trained personnel
Deflating air pillow	General patient population Nervous or excited horses Not well trained horses Horses undergoing prolonged anesthesia and anticipated muscle weakness	Prevents premature attempts to rise improving quality of recovery Does not require special training of personnel	Additional expenses for air mattress and fan Requires removal of horse shoes to prevent puncture of air pillow
Large-animal vertical lift – Large Animal lift/Becker Sling[1] – UC Davis Large Animal Lift[2]	Old and fatigued horses Heavy (draft and large Warmblood horses) Horses with mild to moderate neuropathies and/or myopathies	Lightweight equipment Easy to put on down horse Simple to use	Requires overhead hoist in recovery stall Requires cooperative animal Risk of tissue strangulation if narrow girths are used Requires trained personnel

Table 22.2 (*cont'd*)

Method of assisted recovery	Group of horses for which technique is suitable	Advantages	Disadvantages/Complications
Sling recovery – Sling–shell system – Liftex Sling[3] – Anderson Sling[4]	Horses undergoing major orthopedic surgery (esp. long-bone fracture repair) Horses with major soft tissue trauma Horses with neuropathies Muscle fatigued horses Horses in poor body condition	Prevents excessive weight loading in affected limb Prevents injuries related to muscle fatigue or neuronal/motor dysfunction Dependent on sling design; useful for long-term support of patient in recovery period (e.g. Anderson Sling) Significantly lower cost and less manpower required compared with pool recoveries	Requires overhead hoist(s) Requires cooperative animal Usually difficult to put on down horse Rolling out of sling if sling doesn't match body size Uneven body support (except Anderson Sling) May limit chest excursions and thus breathing similar to a corset (esp. Liftex Sling) Requires trained personnel
Pool recovery system – Hydro-pool – Pool-raft system	High risk of unstable recovery: – Long-bone, pelvic or scapular fracture – Major soft tissue trauma – Central or peripheral neuronal disease – Horses with bad demeanor – Poor body condition	Significantly reduced incidence of recovery injuries to musculoskeletal apparatus in patients of the highest risk categories Pool systems can also be used for physical therapy	Risk of pulmonary edema (Hydro-pool) Risk of incisional infections (esp. in Hydro-pool) Wet casts or bandages Expensive to use and maintain Labor intensive Horse size limitations based on pool and/or raft size Longer recovery time Requires trained personnel

[1] Large Animal Lift/Becker Sling: Häst, PSC, 10 300 Wingfield Lane, Louisville, KY 40291-3655, USA; phone: (502) 267-7685 or 1-888-924-7685; fax: (502) 267-1395; http://www.hast.net

[2] UC Davis Large Animal Lift (LAL): manufactured by Charles Anderson; distributed by Large Animal Lift Enterprises, 1026 Marchetti Court, Chico, CA 95926, USA; phone: (530) 320-2627; http://www.largeanimallift.com

[3] Liftex Sling: Liftex, Inc., 443 Iviland Rd., Warminster, PA 18974, USA; phone (215) 957-0810; fax: (215) 957-9180; http://www.liftex.com

[4] Anderson Sling: manufactured by Charles Anderson; distributed by Care for Disabled Animals/CDA Products, 18 385 Van Arsdale Road, Potter Valley, CA 95469, USA; phone: (707) 743-1300; fax: (707) 743-2530

Table 22.3 Criteria for selecting method of assisted recovery.

Factors involved in selecting type of assisted recovery system

Patient-related factors:
    Size, weight, age, body condition
    Temperament and training status

Injury- and/or disease-related factors:
    Type and extent of soft tissue trauma
    Type of fracture and extent
    Presence of neuronal deficits affecting proprioception and/or motor function
    Presence of central neurological disease (e.g. history of seizure activity)

Surgery-related factors:
    Surgical technique used
    Site and invasiveness of surgical procedure
    Location and size of cast or bandage
    Degree of surgery-related tissue trauma

Anesthesia-related factors:
    Anesthetic protocol and drugs used (inhalant anesthesia, TIVA, balanced anesthesia)
    Duration of anesthesia
    Analgesia protocol used and adequacy of intraoperative pain control
    Options for postoperative/prerecovery analgesia
    Occurrence of intraoperative complications (e.g. severe cardiopulmonary dysfunctions)

Facility-related factors:
    Layout/design of available recovery stall
    Availability of equipment for assisted recovery techniques
      Ropes
      Mattress (size and thickness)
      Slings/animal lifts (type and size)
    Availability and type of specially designed recovery systems

Personnel-related factors:
    Manpower
    Familiarity with techniques of assisted recovery

A. Personnel within recovery stall assisting horse manually

- o The concept is to keep the horse in lateral recumbency as long as possible (i.e. until signs indicate that the horse has regained sufficient mental function and muscle strength).
- o The method does not require special equipment but is not without risk to personnel.
- o *Only personnel familiar with recoveries should be allowed to 'hand-recover' horses.*

Technique
- o An experienced attendant kneels behind the horse's head with one knee pushing on its neck and both hands holding its head, raising the horse's nose and stretching it backwards.
  - – Restraining the head prevents the horse from swinging its head ventrally, thus preventing the horse from moving into sternal recumbency.

- ○ A second person, if available, may stand behind the croup of the horse and grasp the tail at the moment the animal is allowed to get up.
- ○ *Pre-recovery sedation* and *analgesia* are often helpful to minimize struggling in the early postanesthetic period, and the effects usually last 15–40 min.
- ○ Once the horse is judged to be awake (i.e. by cessation of nystagmus, return of normal tongue tone, chewing, normal responses to environmental stimuli), it should be allowed to roll sternal.
  - – In this position, the two attendants may or may not be able to control the movement of the horse.
- ○ Once standing, the attendants should take hold of the halter and tail to keep the horse from moving until it has regained sufficient coordination to walk safely.
- ○ Most horses stand within an hour of discontinuing anesthetic drug administration.

B. Head and tail rope recovery (see Fig. 22.1)

- ○ The method is very similar to manual assistance described above and is based on the same concept.

Requirements
- ○ The corners (or opposite walls) of the recovery stall must be equipped with recessed rings and/or front and hind doors of recovery stall must have holes through which head and tail rope can be passed.
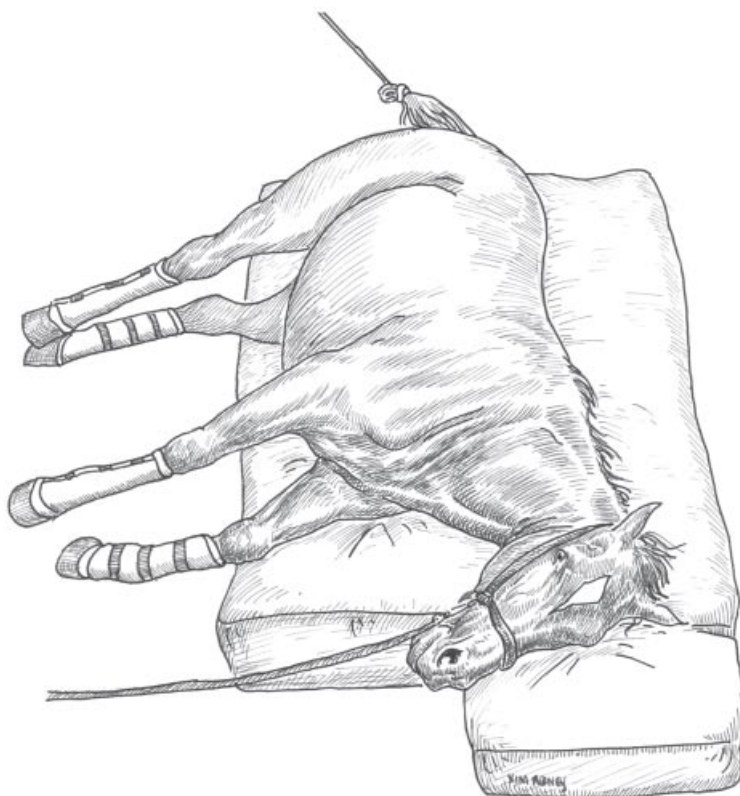
Fig. 22.1   Use of a foam rubber mattress and head and tail ropes to assist a horse during recovery from anesthesia. The bottom front leg is pulled forward to lessen pressure on the dependent limb, and all lower limbs are protected with gaiters against injury. The horse is positioned so that it will roll off the mattress as it moves into sternal recumbency.

    o Ropes should be strong but flexible enough to allow tying of knots for secure attachment to head (or halter) and tail and to ensure smooth gliding through rings and/or door holes.

Technique

    o Once the horse is considered to be awake, the attendant leaves the position behind the head and allows animal to stand up when it next tries.

    o Two or more helpers can assist the horse in rising from lateral to sternal to standing by pulling on the ropes while keeping a safe distance from the recovering horse.

    o Strain on head and tail rope provides some balance and support for the horse.

        – Tension on the *head rope* decreases the incidence of head strikes against walls or floor should the horse struggle.

        – Tension on the *tail rope* reduces forward momentum of the horse as it tries to stand.

    o Once the horse is standing, head and tail ropes help keep it steady.

    o This technique restricts the horse from using more than a third of the recovery stall.

C. Deflating air pillow

    o Recovery of horses on an air cushion significantly improves recovery quality.

    o The concept behind the technique is to keep the horse recumbent until adequate mentation and muscle strength have returned.

    o The method is safe and without risk to personnel.

Technique

    o A rapid inflation–deflation air pillow that is 46 cm (18 inch) thick is placed on top of a thick foam mat covering the entire recovery-stall floor.

    o Following surgery, the anesthetized horse is placed in the center of the recovery stall on the deflated air mattress.

    o The pillow is rapidly filled with air from a fan located outside the recovery stall, pumping air continuously through a hose-like duct into the mattress.

        – The soft pillow hinders the horse from rolling sternal and protects it from harming itself or causing pressure injury to dependent nerves and muscles.

    o Once the horse is adequately awake, the fan is switched off and two 92-cm (36-inch) zippers along the sides of the air mattress are opened to allow for rapid deflation.

    o When the air pillow is flat, the horse can attain sternal recumbency and safely stand.

D. Large-animal vertical lift (LAL) (see Fig. 22.2)

    o The LAL was developed very recently as a robust but simple and lightweight device for assisting horses to stand.

    o It can be easily placed on a recumbent horse.

    o Principal components are an aluminum spread bar (keeps the front and rear parts of the lift separated), to which chest and body slings are attached and which can handle body weights up to 1000 kg (2200 lb).

    o LALs are particularly helpful in assisting very heavy and/or muscle-fatigued horses.
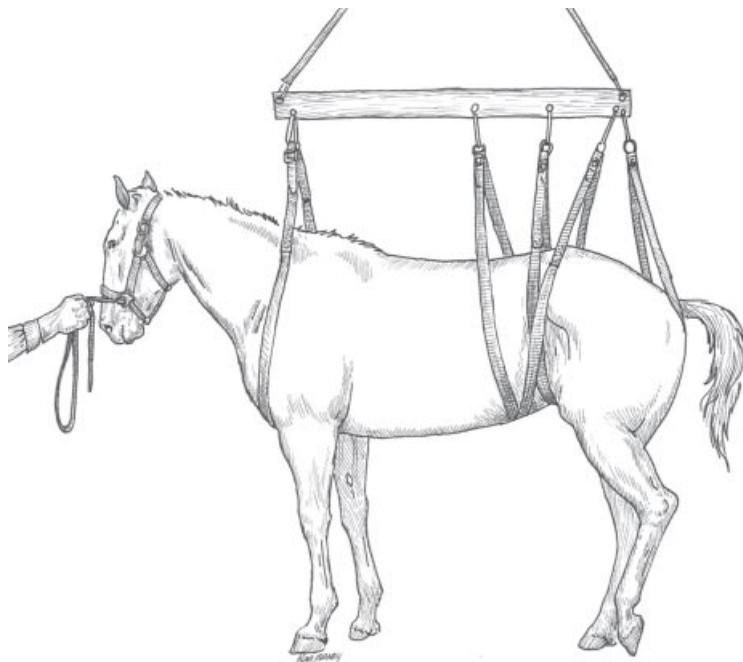
Fig. 22.2 Assisted recovery with the aid of a large-animal vertical lift. As the horse attempts to move from lateral to sternal recumbency, it is lifted off the ground into a standing position with the head and tail rope helping to stabilize the patient during this process. (Reproduced courtesy of the University of California–Davis.)

E. Sling recovery

o The high incidence of musculoskeletal system injury during recovery has stimulated the design of various sling systems in which the anesthetized horse may be placed.
o Slings are used commonly for recovery of the following types of cases:
  – Horses undergoing major orthopedic surgery in which any misstep or excessive weight loading of the affected limb may lead to implant failure.
  – Horses that have an external skeletal fixation device or transfixation cast.
  – Horses with neurological or motor dysfunctions.
  – Horses in poor body condition.

Technique
  o The sling is placed on the horse when it is still anesthetized or very sedate.
    – Should the decision to use a sling be made after the horse has tried to stand, it should be re-anesthetized or heavily sedated unless the horse is very calm and cooperative.
  o Allow the horse to slowly wake up from sedation 60 min after the end of anesthesia.
    – Treatment with an α_2 agonist should be considered to keep the horse deeply sedated and pain-free while allowing time for elimination of residual anesthetic.
    – If the recovery becomes prolonged, an α_2 antagonist (*yohimbine* 0.05–0.10 mg/kg, IM; or *atipamezole* 0.05–0.10 mg/kg, IM) may be given.
  o Once the horse looks bright and is making an attempt to get up, it should be lifted in the sling with four legs being raised just off the ground and then lowered again.
    – An awake horse will stand as soon as its feet contact the ground.
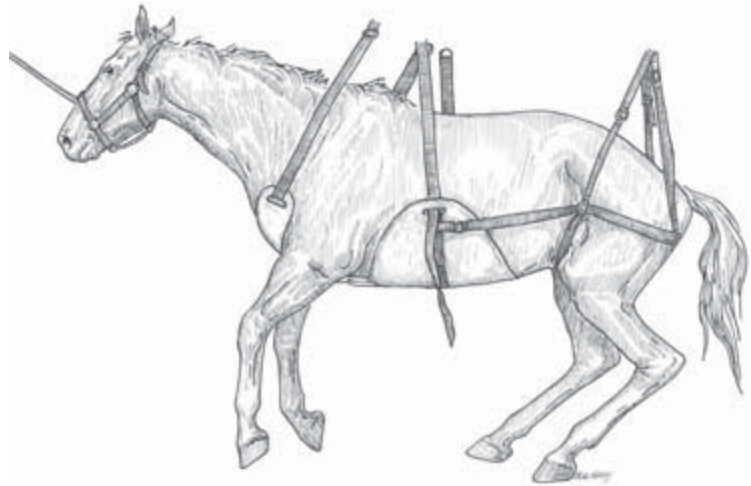
Fig. 22.3   Sling-shell system
and with horse recovering in it.
(Reproduced courtesy of Prof. Urs
Schatzmann, University of Berne,
Switzerland.)

Available sling systems
1. Sling-shell recovery system (see Fig. 22.3)
    o   This system was developed at the University of Berne.
    o   The sling system is suspended on four hoists affixed to overhead rails.
    o   Two customized glass-fiber enhanced plastic shells that match the contour of the front
        breast and the ventral part of the thorax support most of the horse's weight in the front
        without causing pressure damage to blood vessels or nerves or impairing expansion
        of the rib cage during breathing.
    o   Transverse girths passing in front of and behind the thighs support the rear of the body.
    o   Transverse girths and straps attached to the edges of the shells and hooked up on to
        the hoists stabilize the body on the side.
    o   The sling system is easily mounted on the anesthetized horse after rolling the horse
        into dorsal recumbency for placement of breast and ventral thorax shells, and back
        into lateral recumbency for attachment of girths and straps to the four hoists.

2. Liftex large animal sling (see Fig. 22.4)
    o   Most widely used sling.
    o   Commonly used for horses with major musculoskeletal trauma prior to surgery for
        safe induction of anesthesia and transport to the surgery table.
    o   Important features of its design:
        –   It is difficult for the horse to back out of the sling or dog-sit in it.
        –   Made of breathable nylon fabric that reduces sweating.
        –   Can be adjusted to fit horses of different sizes.
        –   Fulcrum of suspension from the lifting rings can be adjusted to promote sternal
            versus abdominal support (point of lifting of the sling should be over the withers).
        –   Offers flexibility in handling horses with injured shoulders or humeral fractures.

        Note: May impair breathing by acting like a narrow corset when horse is lifted to a
        standing position.

3. Anderson sling (see Fig. 22.5)
    o   Specially designed sling system attached to a metal frame that can be affixed to either
        an overhead hoist or a hydraulic apparatus with a power supply.
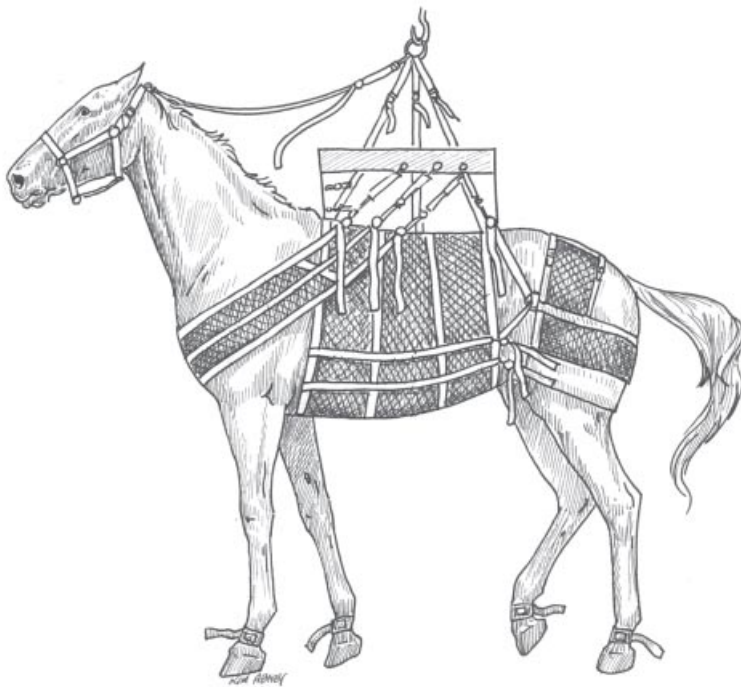
Fig. 22.4 Liftex large animal sling. (Reproduced courtesy of Liftex, Inc., Warminster, PA.)
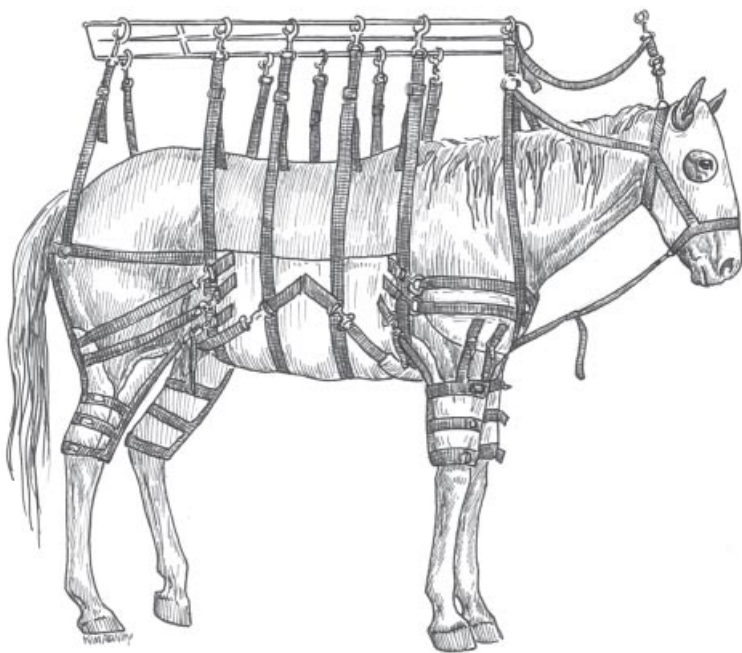
Fig. 22.5 Horse in Anderson sling. (Reproduced courtesy of Charles Anderson and the University of California–Davis.)

- ○ Useful for lifting and stabilizing a horse waking up from general anesthesia.
- ○ Has *distinct advantages* over other slings:
  - – Supports the animal from the skeletal system (not by its chest and abdomen).
  - – Distributes the horse's weight much more evenly.

- More comfortable for the horse.
- Doesn't interfere with muscle, nerve or respiratory function.
  - Hydraulically controlled overhead frame provides an option for finely adjusting the weight distribution between front and rear as well as left and right limbs.
    - Allows a horse to bear weight on only the front or rear limbs, or to adjust it to have only three limbs bear weight while one limb is kept suspended and restrained.
  - Horses can be kept in the sling for extended periods of time (weeks to months).

F. Pool recovery

- o Recovery in a pool system may offer advantages over recovery in a sling system.
- o It can be lifesaving in horses that are at extremely high risk of unstable recovery due to the nature of the original trauma, prolonged and complicated surgical procedure, central or peripheral neuronal disease, and/or temperament.
- o Two pool recovery systems are currently in use.

Available pool systems
1. Hydro-pool (Fig. 22.6)
- o Uses a rectangular water pool approximately 3.7 m long, 1.2 m wide, and 2.6 m deep ($12 \times 4 \times 8.5$ ft) and equipped with a hydraulic, stainless steel grate floor that can be rapidly raised or lowered.
- o Water is heated to 32–37°C (90–100°F) to avoid hypothermia.
- o After surgery, the still anesthetized and intubated horse is lifted into the pool using a large animal sling or net and an overhead rail and hoist system.
- o Two ropes are attached to the halter for subsequent cross-ties to support and restrain the head.
- o The horse is then lowered into the pool with the body completely submerged.
- o An air-filled tire inner tube is placed around the upper neck or, preferably, an air-filled flotation device is placed *in front of* the neck, allowing the horse to rest its head without risk of aspirating water or drowning.
- o The sling or net remains in place but is not bearing weight.
- o An α_2 agonist (e.g. *xylazine*) may be administered for sedation.
- o Once the horse is judged to be awake, the floor of the pool is raised until it touches the horse's hooves, allowing the horse to bear some weight.
- o If the horse demonstrates sufficient weight-bearing capability, the pool floor is raised further until the water level reaches the mid-thorax.
- o At this point the inner tube or air-filled flotation device, cross-tie head ropes, and sling or net are removed.
- o Finally, the floor is lifted to ground level and the horse walked from the recovery pool to a warm stall.
- o *Precautions and concerns:*
  - Wound closure requires extra effort to provide a multilayered, water-tight closure.
    - Use of cyanoacrylate glue spray enhances effectiveness of waterproof closure.
    - Water-repellant bandage and cast material must be used.
  - Pulmonary edema (up to 17% incidence) is the most common complication reported.
  - Horse may suffer skin abrasions when moving vigorously.
  - Horse may attempt to exit the pool if anxious, intolerant of the pool, or awake.
  - Horse must be dried after removal from pool.

Fig. 22.6   Horse submerged in Hydro-pool. (Reproduced courtesy of Biomedical Communications Unit, College of Veterinary Medicine, Washington State University.)

2. Pool-raft system (see Fig. 22.7)
   o Uses a circular pool 6.7 m (22 ft) in diameter, 3.4 m (11 ft) deep, and surrounded by a cantilevered deck.
   o Water is heated to 36°C (96°F).
   o After surgery, the anesthetized horse is lifted using a large animal sling and overhead monorail/hoist system.
   o The horse is lowered into a large raft modified to accommodate the limbs and equipped with an additional air-cushion attachment at the front to protect the head from striking the pool deck or sinking into the water.
   o Once correctly positioned in the raft, horse and raft are lowered into the pool using two separate hoists (one carrying the horse in the sling, one carrying the raft).

Fig. 22.7   Horse floating in Pool raft and then lifted out of the raft to the recovery stall.

- o The raft is secured to rings on the pool deck, while the horse's head is secured using cross-tied head ropes.
- o Sedation or tranquilization with *xylazine* or *acepromazine* may become necessary if the horse shows signs of severe anxiety or excitement early during the pool recovery phase or immediately before transfer from the pool to the recovery stall.
- o Once fully awake, the horse is blindfolded and lifted out of the raft and transferred to a nearby recovery box.
- o *Advantages* of this specific recovery system over the hydro-pool system include:
  - – Use of a flotation device avoids complications associated with complete or partial water submersion of the animal's body.
  - – Wounds and wound bandages/casts are less likely to get wet, reducing the risk of incisional infection.
  - – Significantly lower, if any, risk for pulmonary edema.
  - – Faster average recovery time.
  - – Little risk of acquiring leg injuries while in pool raft.

23 Euthanasia

Ron Jones

- Euthanasia is often defined as a 'quiet and gentle death' but it is probably better to refer to it as a 'quick and painless' death.
- Euthanasia is carried out by veterinarians under three different circumstances:
  - At *sporting events* when it is not feasible to treat a particular injury such as compound fractures or fractures of the proximal long bones of the limbs.
  - When horses have reached the end of their useful and productive life and are suffering from *crippling, debilitating, or untreatable conditions*.
  - When *incurable conditions are discovered during surgery* and the horse is not allowed to recover from anesthesia.
- Each of the three situations demands a different approach and requires different personal skills in dealing with the owners and attendants.
- In most countries, euthanasia of an animal is not considered to be an act of veterinary surgery and hence can be performed by non-veterinarians.

I. Important considerations

A. Insurance

- It is important to ascertain whether the animal is insured and, wherever possible, to seek permission from the insurance underwriters.

B. Permission

- If the owner of the horse or a responsible agent is available, it is best to seek permission to carry out euthanasia.

C. Second veterinary opinion

- In an emergency and in the absence of the owner or agent, it is strongly recommended that the indications for euthanasia be documented by a second veterinarian.

D. Welfare issues

- In all situations it is important to stress that the welfare of the horse is the primary consideration.

E. Written consent

o   Under most circumstances it is preferable to obtain written consent.

F. Verbal consent

o   Under certain circumstances, a verbal agreement in the presence of a *reliable witness* is adequate.

G. Written records

o   It is important to keep written records of the procedure.

H. Postmortem examination

o   A postmortem examination should be carried out whenever possible.

II. The ideal euthanasia solution

- Should produce relaxation allowing the horse to become recumbent in a natural manner and avoid crashing to and thrashing around on the ground.
- Is easy to administer in a relatively *small volume* through a relatively *small-bore* needle.
- Is capable of being administered as a *single dose*.
    o   Placement of a catheter is recommended to avoid repeated venepuncture and/or perivascular deposition of drug.
- Must be 'reasonably safe' for the personnel.
- *Works with certainty* on every occasion.
- Must not produce unpleasant and undesirable signs such as twitching, vocalising, or gasping.
- Inexpensive.

III. Techniques

- Horses can be humanely killed by using either:
    o   *Drugs* which produce hypoxia or depress the central nervous system.
    o   *Physical methods* which damage the brain.
- Irrespective of the technique, the aim is to stop the flow of oxygenated blood to the vital tissues and produce death.

A. Hypoxia-inducing agents

o   Include muscle relaxants such as *succinylcholine*.
o   Should never be used as sole agents as that would be inhumane.
    –   They produce muscle paralysis *without anesthesia*.
o   Should be used in combination with an anesthetic drug (e.g. a barbiturate).

B. CNS depressants

- ○ *Agents of choice* for euthanasia of horses.
- ○ Produce cardiac and respiratory arrest.
- ○ Due to the horse's physical size, some agents (e.g. inhalational drugs) are impractical.
- ○ Inhalational drugs are rarely used.
  - – An exception is their occasional use to kill an already anesthetized animal.

Barbiturates
- ○ Probably the *drugs of choice* for euthanasia.
- ○ Have a rapid onset of action.
- ○ Effect is dose-related.
  - – 20–30 mg/kg or twice the dose required to produce anesthesia.
- ○ Their action is relatively smooth with minimal discomfort.
- ○ Administered IV in relatively small volumes.

Note: Prior sedation with an α_2 agonist may slow the circulation and produce an unexpected and undesirable response.

Chloral hydrate
- ○ Has a relatively *slow onset* of action.
- ○ Large volumes are required to produce anesthesia and death.
  - – Approximately three times the anesthetic dose.
- ○ *Not recommended as the sole agent*, although it can be used in the anesthetized horse.
- ○ Saturated solutions may be used with *succinylcholine* (100–200 mg, IV) added to reduce the agonal responses.
- ○ Can also be used with magnesium sulphate and/or barbiturates.

Magnesium sulfate
- ○ Should *not be used as a sole agent* for euthanasia.
- ○ Its main use is in combination with *chloral hydrate* and/or barbiturates.

Potassium chloride
- ○ Can produce cardiac arrest rapidly followed by death due to hypoxia.
- ○ It must *not be used as a sole agent* as it does not produce anesthesia.
- ○ Its use is limited to the unconscious or anesthetized animal.

C. Physical methods of euthanasia that result in brain damage

Free bullet
- ○ In some countries *shooting with a free bullet* has been widely used.
- ○ When using a gun it is important to place the muzzle in the correct position.
  - – The muzzle is placed just above the intersection of imaginary lines drawn from the base of the ear to the orbit on the opposite side of the head.
- ○ Horses are usually sedated beforehand.

Captive bolt
- ○ Generally not a practical or suitable method for use in the horse.

IV. Recommended techniques

- In general it is preferable to perform euthanasia out of the sight of the public.
  - This can be achieved by moving the animal, preferably after the administration of sedative and analgesic drugs, out of public view.
  - Screens may also be used to conceal the horse.
- In the presence of a concerned owner, it may be desirable to induce anesthesia using a common technique (e.g. α_2 agonist followed by *diazepam*/*ketamine*) prior to administration of the euthanasia agent (e.g. barbiturate).
  - This will ensure that unconsciousness is attained in a tranquil, relaxed, and reliable manner.
- Proper *restraint* of the head is essential and a suitable head collar or bridle should be used.

A. Thiopentone sodium

- This technique has found universal favor.
- Dose: 10 g dissolved in 60 ml of water.
- It is administered IV through a 14-gauge catheter.
  - It is followed immediately by *succinylcholine* (100 mg).
- If death does not occur within 2 or 3 min, 50 ml of *pentobarbitone* (200 mg/ml) should be administered IV.

Note: The use of α_2 agonists for sedation is *not recommended* as they slow the circulation and the horse tends to fall over backwards.

B. Pentobarbitone

- 100 ml of triple-strength solution followed by *succinylcholine* (IV) has also been recommended.

C. Quinalbarbitone and nupercaine

- This combination of a barbiturate and a local anesthetic is available as a commercial mixture in some countries and is widely used for euthanasia of horses.
  - In the UK, it is subject to the *Misuse of Drugs* regulations and to special prescription and record keeping but not to custody requirements.
- A dose of 5 ml/50 kg is recommended to be administered rapidly (12–15 seconds) IV through a catheter.
- This combination has the advantage of a *small volume* and a relatively *rapid rate of action*.

Note: The use of α_2 agonists is *not recommended* except in a fractious horse or when sedation is essential for assessment prior to euthanasia.

V. Confirmation of death

- Death should always be confirmed before leaving the scene.
- This is done by noting:
    - The absence of *corneal reflexes*.
    - The absence of *cardiac and respiratory activity*.
    - The presence of *muscle relaxation*.

Index